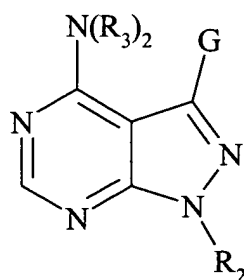


CLAIMS

We claim:

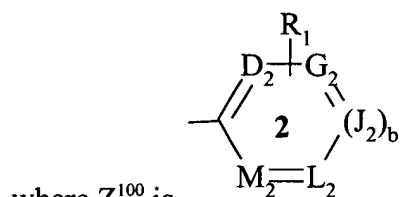
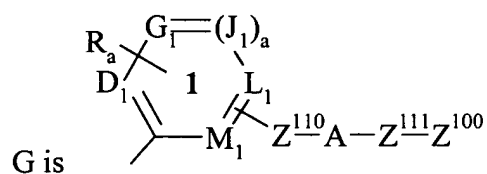
1. A compound of Formula (I)

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(I)

- 10 racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



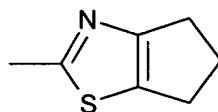
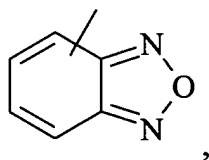
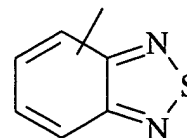
where Z^{100} is or a group optionally substituted with R_1 selected

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from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-

a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,



5

, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

10

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

15

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted

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phenyl;

R_a and R_i each represent one or more substituents for each occurrence

independently selected from the group consisting of hydrogen, halogen, -

CN, $-\text{NO}_2$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{H}$, $-\text{OH}$, $-\text{C}(\text{O})\text{O-alkyl}$, $-\text{C}(\text{O})\text{O-aryl}$, -

5 $\text{C}(\text{O})\text{O-heteroaryl}$, $-\text{C}(\text{O})\text{-alkyl}$, $-\text{C}(\text{O})\text{-aryl}$, $-\text{C}(\text{O})\text{-heteroaryl}$, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl,

substituted or unsubstituted cycloalkyl, substituted or unsubstituted

alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted

10 heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroarylalkoxy, substituted or

unsubstituted arylalkoxy, substituted or unsubstituted alkyl- $\text{S}(\text{O})_p$ -,

substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-

15 $\text{S}(\text{O})_p$ -, substituted or unsubstituted heteroaryl- $\text{S}(\text{O})_p$ -, substituted or

unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl,

substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted

alkynyl, substituted or unsubstituted amino, substituted or unsubstituted

aminoalkyl, substituted or unsubstituted amido groups, substituted or

20 unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-\text{Z}^{105}$ -

$\text{C}(\text{O})\text{N}(\text{R})_2$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-C}(\text{O})\text{-Z}^{200}$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-S}(\text{O})_2\text{-Z}^{200}$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-}$

$\text{C}(\text{O})\text{-N}(\text{R})\text{-Z}^{200}$, R_c and CH_2OR_c ;

where R_c for each occurrence is independently hydrogen, substituted or

unsubstituted alkyl, substituted or unsubstituted aryl, $-\text{CH}_2\text{-NR}_d\text{R}_e$, -W-

25 $(\text{CH}_2)_t\text{-NR}_d\text{R}_e$, $-\text{W-(CH}_2)_t\text{-O-alkyl}$, $-\text{W-(CH}_2)_t\text{-S-alkyl}$, or $-\text{W-(CH}_2)_t\text{-OH}$;

Z^{105} for each occurrence is independently a covalent bond or $(\text{C}_1\text{-C}_6)$;

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6), substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl; or R_d , R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or NR_f , wherein R_f for each occurrence is independently H or alkyl; or

R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

A is $-(C_1-C_6)-$, $-O-$, $-S-$, $-S(O)_p-$, $-N(R)-$, $-N(C(O)OR)-$, $-N(C(O)R)-$, $-N(SO_2R)-$, $-CH_2O-$, $-CH_2S-$, $-CH_2N(R)-$, $-CH(NR)-$, $-CH_2N(C(O)R)-$, $-CH_2N(C(O)OR)-$, $-CH_2N(SO_2R)-$, $-CH(NHR)-$, $-CH(NHC(O)R)-$, $-CH(NHSO_2R)-$, $-CH(NHC(O)OR)-$, $-CH(OC(O)R)-$, $-CH(OC(O)NHR)-$, $-CH=CH-$, $-C(=NOR)-$, $-C(O)-$, $-CH(OR)-$, $-C(O)N(R)-$, $-N(R)C(O)-$, $-N(R)S(O)_p-$, $-OC(O)N(R)-$, $-N(R)-C(O)-(CH_2)_n-N(R)-$, $-N(R)C(O)O-$, $-N(R)-(CH_2)_{n+1}-C(O)-$, $-S(O)_pN(R)-$, $-O-(CR_2)_{n+1}-C(O)-$, $-O-(CR_2)_{n+1}-O-$, $-N(C(O)R)S(O)_p-$, $-N(R)S(O)_pN(R)-$, $-N(R)-C(O)-(CH_2)_n-O-$, $-C(O)N(R)C(O)-$, $-S(O)_pN(R)C(O)-$, $-OS(O)_pN(R)-$, $-N(R)S(O)_pO-$, $-N(R)S(O)_pC(O)-$, $-SO_pN(C(O)R)-$, $-N(R)SO_pN(R)-$, $-C(O)O-$, $-N(R)P(OR_b)O-$, $-N(R)P(OR_b)-$, $-N(R)P(O)(OR_b)O-$, $-N(R)P(O)(OR_b)-$,

$\text{N}(\text{C}(\text{O})\text{R})\text{P}(\text{OR}_b)\text{O}-$; $-\text{N}(\text{C}(\text{O})\text{R})\text{P}(\text{OR}_b)-$; $-\text{N}(\text{C}(\text{O})\text{R})\text{P}(\text{O})(\text{OR}_b)\text{O}-$, or $-\text{N}(\text{C}(\text{O})\text{R})\text{P}(\text{OR}_b)-$;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

- 5 R_b for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

- 10 in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_b together form a five- or six-membered heterocyclic ring; or A is NRSO_2 and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1; or $\text{Z}^{110}-\text{A}-\text{Z}^{111}$ taken together is a covalent bond; and

R_2 is H or a group of the formula $-\text{Z}^{101}-\text{Z}^{102}$;

- 15 Z^{101} is a covalent bond, $-(\text{C}_1-\text{C}_6)-$, $-(\text{C}_1-\text{C}_6)-\text{O}-$, $-(\text{C}_1-\text{C}_6)-\text{C}(\text{O})-$, $-(\text{C}_1-\text{C}_6)-\text{C}(\text{O})\text{O}-$, $-(\text{C}_1-\text{C}_6)-\text{C}(\text{O})-\text{NH}-$, $-(\text{C}_1-\text{C}_6)-\text{C}(\text{O})-\text{N}((\text{C}_1-\text{C}_6))-$ or a substituted or unsubstituted phenyl group;

Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or unsubstituted cycloalkyl group; a substituted or unsubstituted cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated heterocyclic group; or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, nitro, halo, substituted or unsubstituted (C_1-C_6) , substituted or

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25

- unsubstituted aryl, substituted or unsubstituted -C(O)-alkyl, substituted
 or unsubstituted alkoxy, substituted or unsubstituted -N(R)-(C₁-C₆) -OR,
 substituted or unsubstituted -N((C₁-C₆) -OR)₂, substituted or
 unsubstituted -N(R)-(C₁-C₆) -C(O)₂R, substituted or unsubstituted -(C₁-
 5 C₆) -N(R)-(C₁-C₆) -OR, substituted or unsubstituted -(C₁-C₆) -N(R)-(C₁-
 C₆) -N(R)₂, substituted or unsubstituted -(C₁-C₆) -C(O)N(R)-(C₁-C₆) -
 N(R)₂, substituted or unsubstituted sulfonamido, substituted or
 unsubstituted ureido, substituted or unsubstituted carboxamido,
 substituted or unsubstituted amino, substituted or unsubstituted -N(R)-
 10 (C₁-C₆) -OR, oxo, and a saturated, unsaturated or aromatic, substituted or
 unsubstituted heterocyclic group comprising one or more heteroatoms
 selected from the group consisting of N, O, and S; wherein the nitrogen
 atoms of said heterocyclic group or heterobicyclic group are
 independently optionally substituted by oxo, substituted or unsubstituted
 15 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 heteroaryl, substituted or unsubstituted -C(O)N(R)₂, substituted or
 unsubstituted -C(O)-(C₁-C₆)-N(R)₂, -C(O)-alkyl, -C(O)-aryl, -C(O)-
 heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or
 unsubstituted heteroarylalkyl; or
 20 R₂ is a group of the formula -B-E, wherein B is a substituted or unsubstituted
 cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or
 unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl,
 substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted
 25 alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or
 unsubstituted alkylene, substituted or unsubstituted aminoalkyl,

- substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, a substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted (C₁-C₆)-azacycloalkyl-, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-, substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-, substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino, substituted or unsubstituted arylcarbonylamino, substituted or unsubstituted alkylcarbonylamino or substituted or unsubstituted aryl;
- a is 1 and D₁, G₁, J₁, L₁ and M₁ are each independently selected from the group consisting of CR_a and N, provided that at least two of D₁, G₁, J₁, L₁ and M₁ are CR_a; or
- a is 0, and one of D₁, G₁, L₁ and M₁ is NR_a, one of D₁, G₁, L₁ and M₁ is CR_a and the remainder are independently selected from the group consisting of

CR_a and N, wherein R_a is as defined above;

b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or

5 b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6;

provided that when A is $-\text{N}(\text{R})-$, Z^{110} and Z^{111} are each a covalent bond, and R_2 is
 10 a 3,4-dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, then Z^{100} is not alkyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl or pyrrolidinyl;

provided that when Z^{110} and Z^{111} are each a covalent bond, and R_2 is a 3,4-
 dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, Z^{100} is
 15 a substituted or unsubstituted alkyl, then A is not alkyl, $-\text{O}-$, $-\text{C}(\text{O})-$, $-\text{NHC}(\text{O})-$ or $-\text{C}(\text{O})\text{O}-$;

provided that when $\text{Z}^{110}-\text{A}-\text{Z}^{111}$ taken together are a covalent bond, then Z^{100} is not alkyl;

provided that when $\text{Z}^{110}-\text{A}-\text{Z}^{111}$ taken together are a C_1-C_6 alkyl, then Z^{100} is not
 20 phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, furyl or thienyl; and

provided that when R_2 is a substituted or unsubstituted cyclopentyl, Z^{100} is an substituted or unsubstituted alkyl, Z^{110} and Z^{111} are each a covalent bond, then A is not $-\text{O}-$, $-\text{C}(\text{O})\text{O}-$, or $-\text{N}(\text{R})-$.

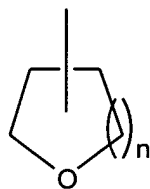
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2. The compound of Claim 1 wherein R_3 is H; R_1 for each occurrence is

independently selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, -CH₂NR_dR_e, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

3. The compound of Claim 1 wherein R₃ is H; R_a for each occurrence is independently selected from the group consisting of F, Cl, Br, I, CH₃, NO₂, OCF₃, OCH₃, CN, CO₂CH₃, CF₃, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, and substituted or unsubstituted styryl.

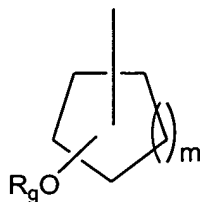
4. The compound of Claim 1 wherein R₃ is H; R₂ is of the formula



wherein n is 1, 2 or 3.

5. The compound of Claim 1 wherein R₃ is H; R₂ is of the formula

-934-



wherein:

m is 0, 1, 2 or 3;

R_9 is H or $-(CH_2)_pN(R_4)R_5$;

5 p is an integer from 2 to 6;

R_4 and R_5 are each, independently, H, azabicycloalkyl or Y-Z;

Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

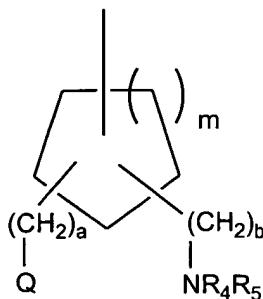
q is an integer from 0 to 6;

10 r is 0, 1 or 2; and

Z is a substituted or unsubstituted moiety selected from the group consisting of alkyl, alkoxy, amino, aryl, heteroaryl and heterocycloalkyl group; or

R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or
15 heterobicyclic group.

6. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein:

m is 0, 1, 2 or 3;

a and b are each, independently, an integer from 0 to 6;

Q is $-OR_6$ or $-NR_4R_5$;

5 each R_4 and R_5 is, independently, H, azabicycloalkyl or Y-Z;

Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

q is an integer from 0 to 6;

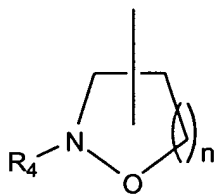
r is 0, 1 or 2; and

10 Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, amino, aryl, heteroaryl or heterocycloalkyl group; or

R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or heterobicyclic group; and

15 R_6 is hydrogen or a substituted or unsubstituted alkyl group.

7. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein:

20 n is 1, 2 or 3;

R_4 is H, azabicycloalkyl or Y-Z;

Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

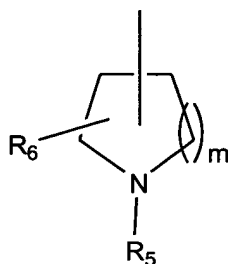
q is an integer 0 to 6;

r is 0, 1 or 2; and

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, aryl,
substituted or unsubstituted heteroaryl or substituted or unsubstituted
heterocycloalkyl group.

5

8. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein;

10

m is 0, 1, 2 or 3;

R_5 is H, azabicycloalkyl or Y-Z;

Y is selected from the group consisting of a covalent bond, -C(O)-, $-(CH_2)_q-$, -

$S(O)_2-$, -C(O)O-, $-SO_2NH-$, -CONH-, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, -

$(CH_2)_qC(O)-$, -C(O) $(CH_2)_q-$ and $-(CH_2)_qS(O)_r-$, where the alkyl portion of

15

$-(CH_2)_q-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, $-(CH_2)_qC(O)-$, -C(O) $(CH_2)_q-$ and -

$(CH_2)_qS(O)_r$ is optionally substituted by a halogen, hydroxy or an alkyl
group;

q is an integer from 0 to 6;

r is 0, 1 or 2; and

20

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino,
substituted or unsubstituted alkoxy, substituted or unsubstituted aryl,
substituted or unsubstituted heteroaryl or substituted or unsubstituted

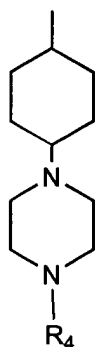
heterocycloalkyl group; or

Y and Z together are a natural or unnatural amino acid, which may be mono- or di-alkylated at the amine nitrogen; and

R₆ represents one or more substituents each independently selected from the group consisting of hydrogen, hydroxy, oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heterocyclylcarbonyl, substituted or unsubstituted aminoalkyl and substituted or unsubstituted arylalkyl;

provided that the carbon atoms adjacent to the nitrogen atom are not substituted by a hydroxy group.

9. The compound of Claim 1 wherein R₃ is H; R₂ is of the formula



wherein:

R₄ is H, substituted or unsubstituted alkyl, substituted or unsubstituted azabicycloalkyl or Y-Z;

Y is selected from the group consisting of -C(O)-, -(CH₂)_q-, -S(O)₂-, -C(O)O-, -

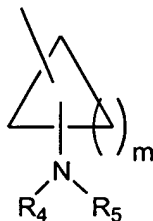
$\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $-(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S}(\text{O})_r-$;

q is an integer from 0 to 6;

r is 0, 1 or 2; and

Z is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

10. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein:

m is an integer from 1 to 6;

R_4 and R_5 are each, independently, H, substituted or unsubstituted azabicycloalkyl or Y-Z;

Y is selected from the group consisting of $-\text{C}(\text{O})-$, $-(\text{CH}_2)_q-$, $-\text{S}(\text{O})_2-$, $-\text{C}(\text{O})\text{O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $-(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S}(\text{O})_r-$;

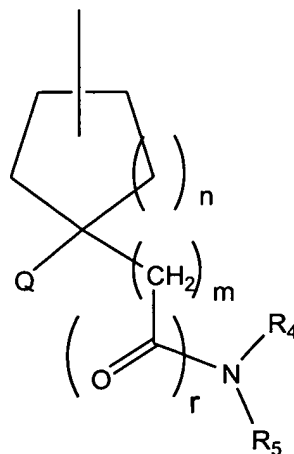
q is an integer from 0 to 6;

r is 0, 1 or 2; and

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterobicyclic group.

11. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein

5

n is an integer from 0 to 4;

r is 0 and m is an integer from 1 to 6; or

r is 1 and m is an integer from 0 to 6;

Q is $-OR_6$ or $-NR_4R_5$;

each R_4 and R_5 is, independently, H, substituted or unsubstituted azabicycloalkyl
or Y-Z;

10

Y is selected from the group consisting of $-C(O)-$, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

q is an integer from 0 to 6;

r is 0, 1 or 2; and

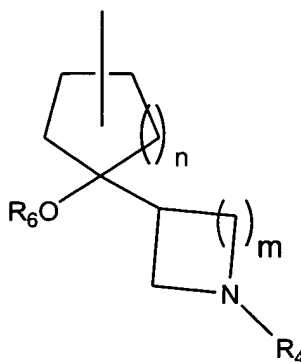
15

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

R_4 , R_5 and the nitrogen atom to which they are attached together form a 3, 4, 5 or

6-membered, substituted or unsubstituted heterocyclic group; and
 R_6 is hydrogen or a substituted or unsubstituted alkyl group.

12. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula



wherein:

n is an integer from 0 to 4;

m is an integer from 0 to 6;

R_4 is H, substituted or unsubstituted azabicycloalkyl or Y-Z;

Y is selected from the group consisting of -C(O)-, $-(CH_2)_q-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $-(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

q is an integer from 0 to 6;

r is 0, 1 or 2;

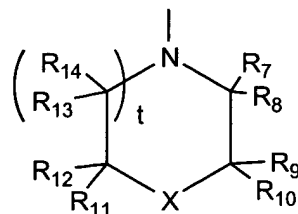
Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl
 or substituted or unsubstituted heterocycloalkyl; and

R_6 is hydrogen or a substituted or unsubstituted alkyl group.

13. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form
 a heterocyclic group of the formula

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wherein:

R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} and R_{14} are each, independently, lower alkyl or hydrogen; or

5 at least one pair of substituents R_7 and R_8 ; R_9 and R_{10} ; R_{11} and R_{12} ; or R_{13} and R_{14} together are an oxygen atom; or

at least one of R_7 and R_9 is cyano, CONHR_{15} , COOR_{15} , $\text{CH}_2\text{OR}_{15}$ or $\text{CH}_2\text{NR}_{15}(\text{R}_{16})$, and

R_{15} and R_{16} are each, independently, H, azabicycloalkyl or V-L;

10 V is selected from the group consisting of $-\text{C}(\text{O})-$, $-(\text{CH}_2)_p-$, $-\text{S}(\text{O})_2-$, $-\text{C}(\text{O})\text{O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S}(\text{O})_r-$;

p is an integer from 0 to 6;

q is an integer from 0 to 6;

r is 0, 1 or 2;

15 L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or R_{15} , R_{16} and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocyclic or a substituted or unsubstituted heterobicyclic group;

20 X is O, S, SO, SO_2 , CH_2 , CHOR_{17} or NR_{17} ;

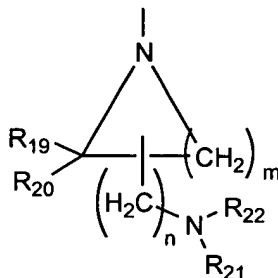
R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-\text{C}(\text{NH})\text{NH}_2$, $-\text{C}(\text{O})\text{R}_{17}$, or -

$C(O)OR_{18}$;

R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and
 t is 0 or 1.

5

14. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocycle of the formula



wherein:

- 10 R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or R_{19} and R_{20} together are an oxygen atom;
- R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L;
- V is selected from the group consisting of $-C(O)-$, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;
- 15 p is an integer from 0 to 6;
- q is an integer from 0 to 6;
- r is 0, 1 or 2; and
- L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or
- 20 R_{21} , R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted

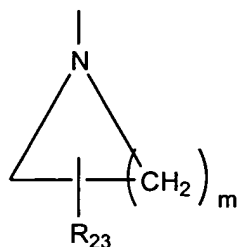
-943-

or unsubstituted heterocyclic group; and

m is an integer from 1 to 6; and

n is an integer from 0 to 6.

- 5 15. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula



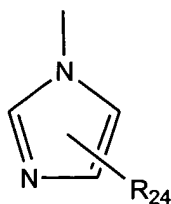
wherein:

m is an integer from 1 to 6;

- 10 R_{23} is CH_2OH , NRR' , $\text{C(O)NRR}'$ or COOR ; and

R and R' are each, independently, hydrogen or substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl.

- 15 16. The compound of Claim 10 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula



wherein:

R_{24} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl,

20 substituted or unsubstituted arylalkyl, carboxyl, cyano, C(O)OR_{25} ,

$\text{CH}_2\text{OR}_{25}$, $\text{CH}_2\text{NR}_{26}\text{R}_{27}$ or C(O)NHR_{26} ;

R_{25} is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl; and

5 R_{26} and R_{27} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L;

V is selected from the group consisting of $-\text{C(O)}-$, $-(\text{CH}_2)_p-$, $-\text{S(O)}_2-$, $-\text{C(O)O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S(O)}_r-$;

p is an integer from 0 to 6;

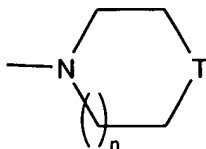
10 q is an integer from 0 to 6;

r is 0, 1 or 2; and

L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or

15 R_{26} , R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.

17. The compound of Claim 10 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula



20

wherein:

T is C(O) , S, SO , SO_2 , CHOR or NR;

R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; and

n is 0, 1 or 2.

18. The compound of Claim 10 wherein:

at least one of R_4 and R_5 is of the formula Y-Z;

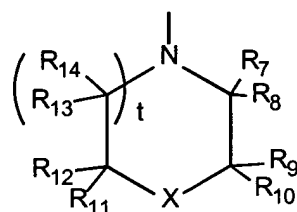
5 Z is of the formula $-N(R_{28})R_{29}$; and

R_{28} and R_{29} are each, independently, substituted or unsubstituted carboxyalkyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted cyanoalkyl; or

R_{28} and R_{29} , together with the nitrogen atom, form a five- or six-membered substituted or unsubstituted heterocyclic group.

15

19. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form a heterocycle of the formula



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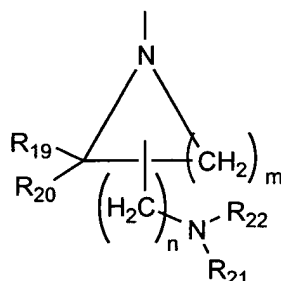
wherein:

R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} and R_{14} are each, independently, lower alkyl or hydrogen; or

at least one pair of substituents R_7 and R_8 ; R_9 and R_{10} ; R_{11} and R_{12} ; or R_{13} and R_{14}

- together are an oxygen atom; or
- at least one of R_7 and R_9 is cyano, CONHR_{15} , COOR_{15} , $\text{CH}_2\text{OR}_{15}$ or $\text{CH}_2\text{NR}_{15}(\text{R}_{16})$; and
- R_{15} and R_{16} are each, independently, H, substituted or unsubstituted
- 5 azabicycloalkyl or V-L;
- V is selected from the group consisting of $-\text{C}(\text{O})-$, $-(\text{CH}_2)_p-$, $-\text{S}(\text{O})_2-$, $-\text{C}(\text{O})\text{O}-$, $-\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S}(\text{O})_r-$;
- p is an integer from 0 to 6;
- q is an integer from 0 to 6;
- 10 r is 0, 1 or 2; and
- L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl; or
- R_{15} , R_{16} and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered,
- 15 substituted or unsubstituted heterocyclic or heterobicyclic group; and
- X is O, S, SO, SO_2 , CH_2 , CHOR_{17} or NR_{17} ;
- R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-\text{C}(\text{NH})\text{NH}_2$, $-\text{C}(\text{O})\text{R}_{18}$, or $-\text{C}(\text{O})\text{OR}_{18}$;
- 20 R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and
- t is 0 or 1.
20. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form
- 25 a heterocycle of the formula

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wherein:

R_{19} and R_{20} are each, independently, hydrogen or lower alkyl; or

R_{19} and R_{20} together are an oxygen atom; and

5 R_{21} and R_{22} are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L;

V is selected from the group consisting of -C(O)-, $-(CH_2)_p-$, $-S(O)_2-$, $-C(O)O-$, $-SO_2NH-$, $-CONH-$, $(CH_2)_qO-$, $-(CH_2)_qNH-$, and $-(CH_2)_qS(O)_r-$;

p is an integer from 0 to 6;

10 q is an integer from 0 to 6;

r is 0, 1 or 2; and

L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or

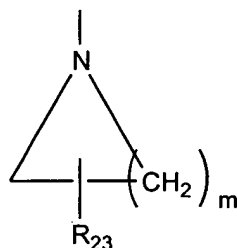
15 R_{21} , R_{22} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group; and

m is an integer from 1 to 6; and

n is an integer from 0 to 6.

20 21. The compound of Claim 11 wherein R_4 , R_5 and the nitrogen atom together form a heterocyclic group of the formula

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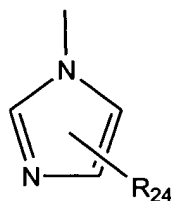
wherein:

m is an integer from 1 to 6; and

R₂₃ is CH₂OH, NRR', C(O)NRR' or COOR;

- 5 R is hydrogen or a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group.

22. The compound of Claim 11 wherein R₄, R₅ and the nitrogen atom together form a heterocyclic group of the formula



10

wherein:

R₂₄ is substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl, carboxyl, cyano, C(O)OR₂₅, CH₂OR₂₅, CH₂NR₂₆R₂₇ or C(O)NHR₂₆;

- 15 R₂₅ is substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclic or substituted or unsubstituted heterocycloaryl group;

R₂₆ and R₂₇ are each, independently, H, substituted or unsubstituted azabicycloalkyl or V-L;

- 20 V is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -

$\text{SO}_2\text{NH}-$, $-\text{CONH}-$, $(\text{CH}_2)_q\text{O}-$, $-(\text{CH}_2)_q\text{NH}-$, and $-(\text{CH}_2)_q\text{S(O)}_r-$;

p is an integer from 0 to 6;

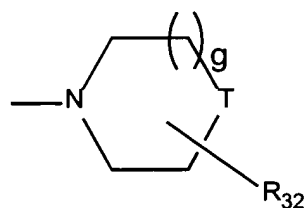
q is an integer from 0 to 6;

r is 0, 1 or 2; and

- 5 L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; or
 R_{26} , R_{27} and the nitrogen atom together form a 3, 4, 5 or 6-membered, substituted or unsubstituted heterocyclic group.

10

23. The compound of Claim 11 wherein at least one of R_4 and R_5 is of the formula Y-Z, wherein Z is of the formula



wherein:

15

g is 0 or 1;

T is C(O) , O, S, SO, SO_2 , CH_2 , CHOR_{17} or NR_{17} ;

R_{17} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, $-\text{C(NH)NH}_2$, $-\text{C(O)R}_{18}$, or $-\text{C(O)OR}_{18}$;

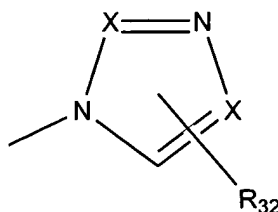
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R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxycarbonyl, substituted or unsubstituted alkoxyalkyl,

it

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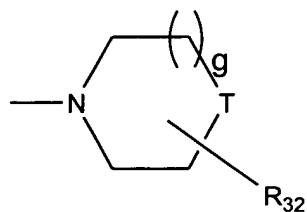
-951-

wherein:

each X is, independently, CH or N; and

R₃₂ is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted or unsubstituted arylalkyl group.

27. The compound of Claim 8 wherein R₅ is Y-Z, wherein Z is of the formula



wherein:

g is 0 or 1;

T is O, S, SO, SO₂, CH₂, CHOR₁₇ or NR₁₇;

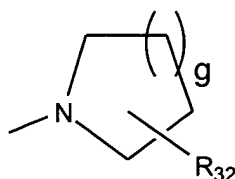
R₁₇ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, C(O)NH₂, -C(NH)NH₂, -C(O)R₁₇, or -C(O)OR₁₈;

R₁₈ is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl; and

R₃₂ is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkylcarbonyl or substituted

or unsubstituted arylalkyl group.

28. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula

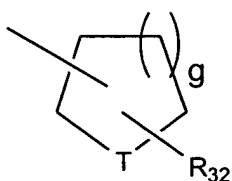


5 wherein:

g is 0, 1 or 2; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkyl carbonyl or substituted or unsubstituted arylalkyl group.

29. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



15 wherein

T is C(O), O, S, SO, SO₂, CH₂, CHOR₁₇ or NR₁₇;

R_{17} is hydrogen, substituted or unsubstituted alkyl, aryl, arylalkyl, -C(NH)NH₂, -C(O)R₁₈, or -C(O)OR₁₈;

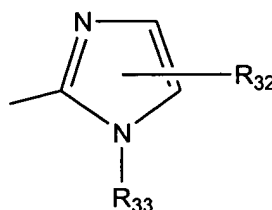
R_{18} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl;

g is 0 or 1; and

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxy alkyl, substituted or unsubstituted hydroxy alkyl, substituted or unsubstituted aminocarbonyl, substituted or unsubstituted alkyl carbonyl or substituted or unsubstituted arylalkyl group.

5

30. The compound of Claim 8 wherein R_5 is Y-Z, wherein Z is of the formula



wherein:

10

R_{32} is hydrogen, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxy alkyl, substituted or unsubstituted hydroxy alkyl, substituted or unsubstituted aminocarbonyl, alkyl carbonyl, substituted or unsubstituted thioalkoxy or substituted or unsubstituted arylalkyl; and

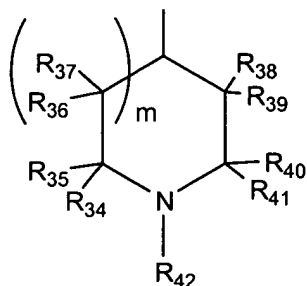
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R_{33} is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted alkoxy alkyl, substituted or unsubstituted aminocarbonyl, perhaloalkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkyl carbonyl or substituted or unsubstituted arylalkyl.

20

31. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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wherein:

m is 0 or 1; and

R₃₄, R₃₅, R₃₆, R₃₇, R₃₈, R₃₉, R₄₀ and R₄₁ are each, independently, methyl or
 5 hydrogen; or

at least one pair of substituents R₃₄ and R₃₅; R₃₆ and R₃₇; R₃₈ and R₃₉; or R₄₀ and
 R₄₁ together are an oxygen atom; and

R₄₂ is H, substituted or unsubstituted azabicycloalkyl or Y-Z;

Y is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -
 10 SO₂NH-, -CONH-, (CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-;

p is an integer from 0 to 6;

q is an integer from 0 to 6;

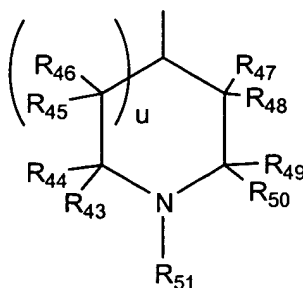
r is 0, 1 or 2; and

Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino,

15 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl
 or substituted or unsubstituted heterocycloalkyl group; or

R₄₂ is of the formula

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wherein:

u is 0 or 1;

R_{43} , R_{44} , R_{45} , R_{46} , R_{47} , R_{48} , R_{49} and R_{50} are each, independently, methyl or
5 hydrogen; or

at least one pair of substituents R_{43} and R_{44} ; R_{45} and R_{46} ; R_{47} and R_{48} ; or R_{49} and
 R_{50} together are an oxygen atom; and

R_{51} is H, substituted or unsubstituted azabicycloalkyl or V-L;

V is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -
10 SO₂NH-, -CONH-, (CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-;

p is an integer from 0 to 6;

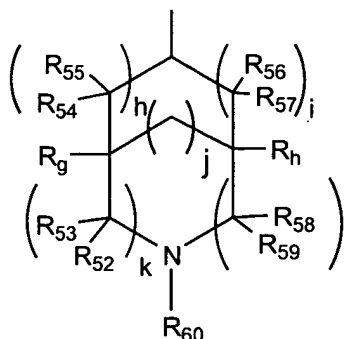
q is an integer from 0 to 6;

r is 0, 1 or 2; and

L is substituted or unsubstituted alkyl, substituted or unsubstituted amino,
15 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl
or substituted or unsubstituted heterocycloalkyl.

32. The compound of Claim 1 wherein R_3 is H; R_2 is of the formula

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wherein:

h, i, j, k and l are independently 0 or 1;

R₅₂, R₅₃, R₅₄, R₅₅, R₅₆, R₅₇, R₅₈, R₅₉, R_g and R_h are each, independently, methyl or
 5 hydrogen; or

at least one pair of substituents R₅₂ and R₅₃; R₅₄ and R₅₅; R₅₆ and R₅₇; or R₅₈ and
 R₅₉ together are an oxygen atom; and

R₆₀ is H, substituted or unsubstituted azabicycloalkyl or Y-Z;

Y is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -
 10 SO₂NH-, -CONH-, -(CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-;

p is an integer from 0 to 6;

q is an integer from 0 to 6;

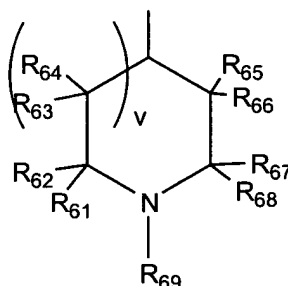
r is 0, 1 or 2; and

Z is substituted or unsubstituted alkyl, substituted or unsubstituted amino,

15 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl
 or substituted or unsubstituted heterocycloalkyl; or

R₆₀ is of the formula

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wherein:

v is 0 or 1;

R₆₁, R₆₂, R₆₃, R₆₄, R₆₅, R₆₆, R₆₇ and R₆₈ are each, independently, lower alkyl or hydrogen; or

at least one pair of substituents R₆₁ and R₆₂; R₆₃ and R₆₄; R₆₅ and R₆₆; and R₆₇ and R₆₈ together are an oxygen atom; and

R₆₉ is H, substituted or unsubstituted azabicycloalkyl or V-1;

V is selected from the group consisting of -C(O)-, -(CH₂)_p-, -S(O)₂-, -C(O)O-, -SO₂NH-, -CONH-, (CH₂)_qO-, -(CH₂)_qNH-, and -(CH₂)_qS(O)_r-;

p is an integer from 0 to 6;

q is an integer from 0 to 6;

r is 0, 1 or 2; and

L is substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl.

33. A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

34. The method of Claim 33 wherein said protein kinase is selected from the group consisting of KDR, FGFR-1, PDGFR β , PDGFR α , IGF-1R, c-Met, Flt-1, Flt-4, TIE-2, TIE-1, Lck, Src, fyn, Lyn, Blk, hck, fgr and yes.
- 5 35. A method of affecting hyperproliferative disorders in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.
- 10 36. A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.
- 15 37. The method of Claim 33 wherein the protein kinase is a protein serine/threonine kinase or a protein tyrosine kinase.
38. A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.
- 20 39. The method of Claim 38 wherein the ulcer or ulcers are caused by a bacterial or fungal infection; or the ulcer or ulcers are Mooren ulcers; or the ulcer or ulcers are a symptom of ulcerative colitis.
- 25 40. A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically

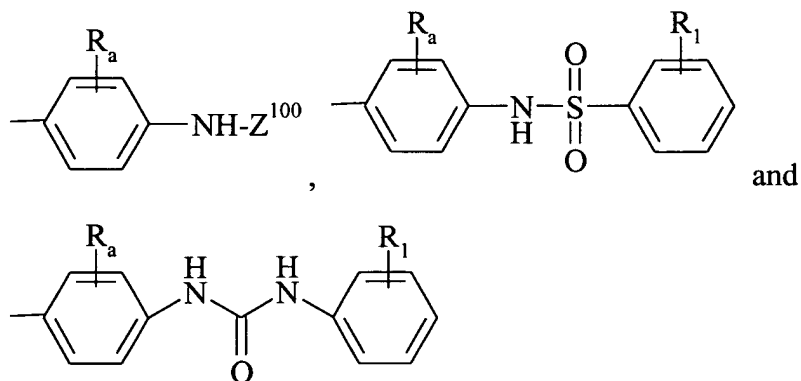
- acceptable salt, prodrug or biologically active metabolites thereof to said patient, wherein said condition is an ocular condition, a cardiovascular condition, a cancer, Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell anaemia, chronic inflammation, systemic lupus, glomerulonephritis, synovitis,
- 5 inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease,
- 10 asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.
- 15 41. The method of Claim 40 wherein the ocular condition is ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or macular degeneration.
- 20 42. The method of Claim 40 wherein the cardiovascular condition is atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion or carotid obstructive disease.
- 25 43. The method of Claim 40 wherein the cancer is a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma,

glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy, Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma, leukemia or malignant ascites.

- 5 44. The method of Claim 40 wherein the diabetic condition is insulin-dependent diabetes mellitus glaucoma, diabetic retinopathy or microangiopathy.
- 10 45. A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 1 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.
- 15 46. The method of Claim 36 wherein the compound or a physiologically acceptable salt, prodrug or biologically active metabolite thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.
- 20 47. The method of Claim 34 wherein the protein kinase is Tie-2.
- 25 48. The method of Claim 46 wherein the compound of Formula I, or physiologically acceptable salt, prodrug or biologically active metabolite thereof, is administered in combination with a pro-angiogenic growth factor.
49. The method of Claim 48 wherein the pro-angiogenic growth factor is selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, VEGF-E, HGF, FGF-1, FGF-2, derivatives thereof and antiidotypic antibodies.

50. The method of Claim 46 wherein the patient is suffering from anemia, ischemia, infarct, transplant rejection, a wound, gangrene or necrosis.
51. The method of Claim 33 wherein the protein kinase activity is involved in T cell activation, B cell activation, mast cell degranulation, monocyte activation, the
5 potentiation of an inflammatory response or a combination thereof.
52. A compound according to Claim 1, wherein:
 R_3 is H;
 R_2 is $-Z^{101}-Z^{102}$,
 Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted phenyl group; and
 Z^{102} is hydrogen, a substituted or unsubstituted alkyl group or a substituted or
10 unsubstituted, saturated or unsaturated heterocyclic group.
53. A compound according to Claim 52, wherein:
 Z^{101} is selected from the group consisting of $-CH_2-C(O)O-$, $-CH_2-C(O)-$, $-CH_2-C(O)-NH-$, $-CH_2-C(O)-N(Me)-$, $-CH(Me)-C(O)O-$, $-(CH_2)_3-C(O)O-$, $-CH(Me)-C(O)-NH-$ and $-(CH_2)_3-C(O)-NH-$;
 Z^{102} is selected from the group consisting of hydrogen, methyl, ethyl, N,N-dimethylaminoethyl, N,N-diethylaminoethyl, 2-phenyl-2-hydroxyethyl, morpholino, piperazinyl, N-methylpiperazinyl and 2-hydroxymethylpyrrolidinyl.
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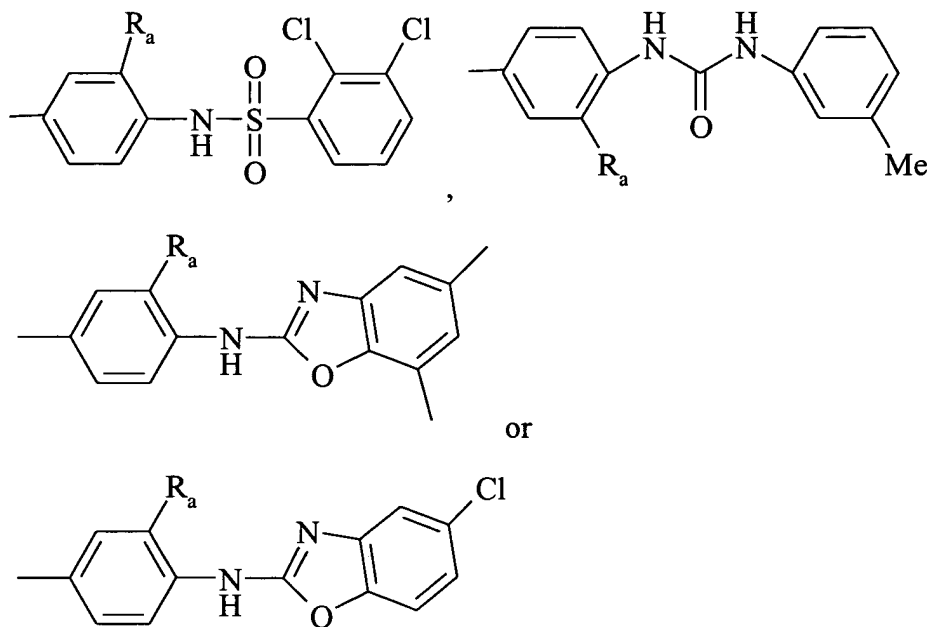
54. A compound according to Claim 53, wherein G is selected from



wherein:

- 5 Z^{100} is a substituted or unsubstituted benzoxazolyl or a substituted or unsubstituted benzthiazolyl.

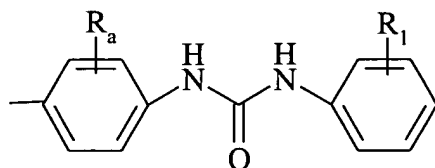
55. A compound according to Claim 8, 9, 10 or 53, wherein G is



wherein there is only one R_a and it is H or F.

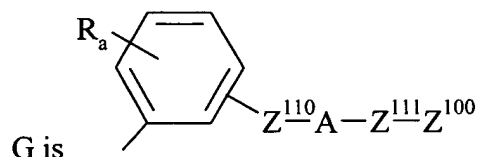
56. A compound according to Claim 52, wherein Z^{101} is a covalent bond; and Z^{102} is an optionally substituted pyridyl.

57. A compound according to Claim 56, wherein G is



5

58. A compound according to Claim 1, wherein R_3 is H; R_2 is cyclopentyl; and



G is

10

59. A compound according to Claim 58, wherein Z^{110} is hydrogen; A is O; and Z^{100} is optionally substituted phenyl, furanyl or thienyl, where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, COOH, NO₂, OMe, -COOMe, OCF₃ and CF₃.

15

60. A compound according to Claim 58, wherein: Z^{110} is hydrogen; A is -O-, -O-(CR₂)_n-C(O)- or -O-(CR₂)_n-O-;

20

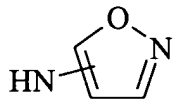
n for each occurrence is 0 to 3;

Z^{100} is an optionally substituted group selected from the group consisting of cyclohexyl, phenyl, tetrahydropyranyl, tetrahydrofuranyl, isoxazolyl and piperidinyl; where Z^{100} is optionally substituted with one or more substituents selected from the group consisting of alkyl, alkoxy, halo, hydroxy and alkoxycarbonyl.

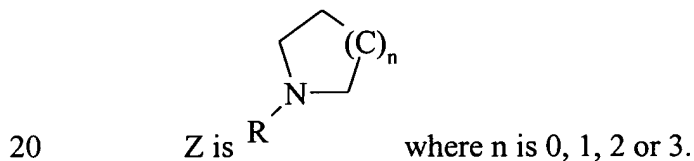
61. A compound according to Claim 58, wherein R^2 is an optionally substituted group selected from the group consisting of cyclobutyl and cyclohexyl.
62. A compound according to Claim 61, wherein R^2 is optionally substituted with one or more substituents selected from the group consisting of hydroxy, alkyl, hydroxyalkyl, carboxyalkyl and phenylalkoxyalkyl.
63. A compound according to Claim 62, wherein G is 4-phenoxyphenyl.
64. A compound according to Claim 6 wherein m is 2; a is 0; R_6 is H; b is 1 or 2; and R_4 and R_5 are each hydrogen.
65. A compound according to Claim 8, wherein m is 0, 1 or 2; R_6 is hydrogen; R_5 is H or Y-Z; Y is a covalent bond, $-C(O)-$, $-(CH_2)_qO-$, $-(CH_2)_q-$, $-(CH_2)_qC(O)-$ or $-C(O)(CH_2)_q-$, where the alkyl portion of $-(CH_2)_qO-$, $-(CH_2)_q-$, $-(CH_2)_qC(O)-$ and $-C(O)(CH_2)_q-$ is optionally substituted by a halogen, hydroxy or an alkyl group; and

Z is hydrogen, alkyl, optionally substituted alkyl, alkoxyalkyl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, or optionally substituted amino.

66. A compound according to Claim 65, wherein:

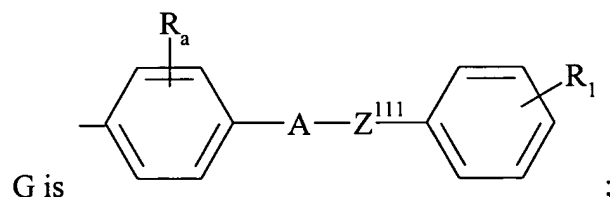
- 5 Z is hydrogen, methyl, ethyl, hydroxymethyl, methoxyethyl, N-methyl-piperidinyl, (t-butoxycarbonyl)(hydroxy)-piperidinyl, hydroxypiperidinyl, (hydroxymethyl)piperidinyl, (hydroxy)(methyl)-piperidinyl, morpholino, (methoxyethyl)piperizinyl, methylpiperizinyl, 4-piperidinylpiperidinyl, imidazolyl, methylimidazolyl, N-methylamino, 10 N,N-dimethylamino, N-isopropylamino, N,N-diethylamino, 2,3-dihydroxypropylamino, 2-hydroxyethylamino, 3-hydroxypropylamino, methoxyethylamino, ethoxycarbonylmethylamino, phenylmethylamino, N-methyl-N-methoxyamino, , furanylmethylamino, piperidinyethylamino, N-(2-N,N-dimethylaminoethyl)-N-methylamino, 15 2-N,N-dimethylaminoethylamino, N-methyl-N-(N-methylpiperidin-4-yl)amino, 2-morpholino-ethylamino, 3-morpholino-propylamino, 3-imidazolylpropylamino, or 3-(2-oxopyrrolidinyl)propylamino.

67. A compound according to Claim 8, wherein m is 2; R₅ is Y-Z; Y is -C(O)-; and



68. A compound according to Claim 9, wherein

R_4 is hydrogen or methyl;



A is selected from the group consisting of O, -N(R)- and -N(R)C(O)-;

Z^{III} is $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$;

5 R is hydrogen or alkyl;

n is 0 to 5;

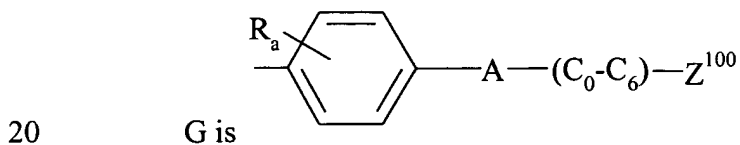
R_a is one or more substituents each independently selected from the group consisting of H, OH, F, Cl, methyl and methoxy; and

10 R_1 is one or more substituents each independently selected from the group consisting of H, CN, F, CF_3 , OCF_3 , methyl, methoxy and an optionally substituted amino group; where said amino group is optionally substituted with one or two groups each independently selected from the group consisting of alkyl, alkoxyalkyl, phenyl, substituted phenyl, and optionally substituted heteroaryl.

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69. A compound according to Claim 68, wherein R_1 is 4-methylphenylthio or 2-pyridinylthio.

70. A compound according to Claim 9, wherein



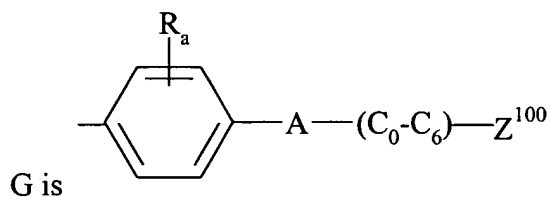
where Z^{100} is selected from the group consisting of benzo[b]thiophene, furanyl

and thiophene.

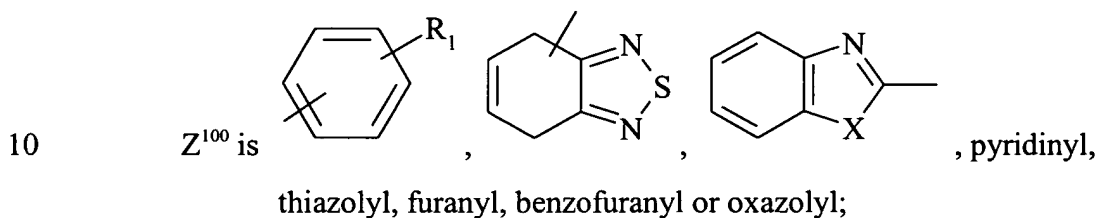
71. A compound according to Claim 9, wherein R_a is alkoxy; A is $-\text{NH}-\text{C}(\text{O})-$; and there is a covalent bond between A and Z^{100} .

5

72. A compound according to Claims 1, 8 or 9, wherein



A is selected from the group consisting of $-\text{N}(\text{R})-\text{C}(\text{O})-\text{N}(\text{R})-$, $-(\text{CH}_2)_n-$, $\text{N}(\text{R})\text{C}(\text{O})\text{N}(\text{R})-$, $-\text{N}(\text{R})-$ and $-\text{N}(\text{R})-\text{SO}_2-$; R is hydrogen or alkyl;



X is S, O or NR^1 where R^1 for each occurrence is independently H or Me;

R_a is one or more substituents each independently selected from the group consisting of H and F; and

15

R_1 is one or more substituents each independently selected from the group consisting of H, F, Cl, Br, NO_2 , CF_3 , alkyl, alkoxy and alkoxycarbonyl.

73. A compound according to Claim 72, wherein:

20

R_4 is methyl;

m is 1, 2 or 3;

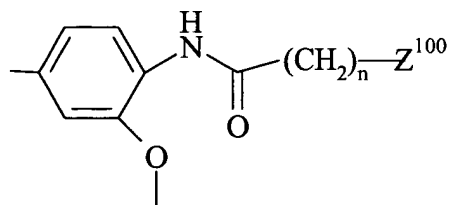
R_5 is Y-Z;

Y is $-C(O)O-$, $-C(O)-$ or $-C(O)-(CH_2)_p-$; and

Z is aminoalkyl, N-alkylamino, N,N-dialkylamino or hydroxyalkylaminoalkyl.

- 5 74. A compound according to Claim 9, wherein

R_4 is methyl;



G is

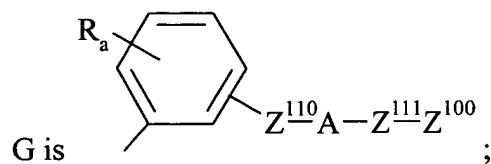
; wherein

n is 0 to 3; and

Z^{100} is an optionally substituted group selected from the group consisting of

- 10 indolyl, indenyl, methylindenyl, methylindolyl, dimethylaminophenyl, phenyl, cyclohexyl and benzofuranyl.

75. A compound according to claim 9, wherein:



G is

;

- 15 Z^{100} is an optionally substituted group selected from the group consisting of phenyl, imidazolyl, indolyl, furanyl, benzofuranyl and 2,3-dihydrobenzofuranyl; where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, CN, optionally substituted alkyl, -O-(optionally substituted

alkyl), $-\text{COOH}$, $-\text{Z}^{105}-\text{C}(\text{O})\text{N}(\text{R})_2$, $-\text{Z}^{105}-\text{N}(\text{R})-\text{C}(\text{O})-\text{Z}^{200}$, $-\text{Z}^{105}-\text{N}(\text{R})-\text{S}(\text{O})_2-\text{Z}^{200}$, and $-\text{Z}^{105}-\text{N}(\text{R})-\text{C}(\text{O})-\text{N}(\text{R})-\text{Z}^{200}$;

Z^{105} is a covalent bond or (C_1-C_6) ;

Z^{200} is an optionally substituted group selected from group consisting of (C_1-C_6) , phenyl and $-(\text{C}_1-\text{C}_6)\text{-phenyl}$;

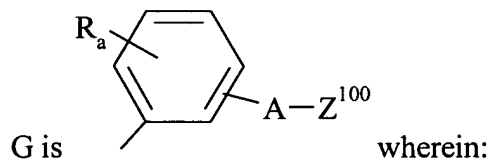
Z^{110} and Z^{111} are each independently a covalent bond or (C_1-C_3) group optionally substituted with alkyl, hydroxy, COOH , CN or phenyl; and

A is O, $-\text{N}(\text{R})-\text{C}(\text{O})-\text{N}(\text{R})-$, $-\text{N}(\text{R})-\text{C}(\text{O})-\text{O}-$, $-\text{N}(\text{R})-$ or $-\text{N}(\text{R})-\text{C}(\text{O})-$, where R is H or alkyl.

10

76. A compound according to Claim 75, wherein R_4 is methyl.

77. A compound according to Claim 8, 9 or 10, wherein



15 Z^{100} is an optionally substituted group selected from the group consisting of benzoxazolyl, benzothiazolyl and benzimidazolyl.

78. A compound according to Claim 77, wherein;

R_4 is methyl;

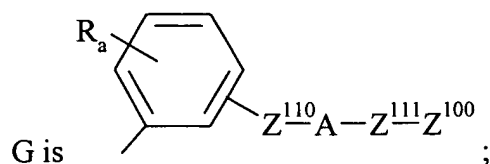
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A is $-\text{NH}-$;

there is only one R_a and it is H or F; and

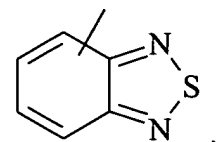
Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of alkyl, halo, CF_3 , and alkoxy.

79. A compound according to Claim 9, wherein:



Z^{100} is an optionally substituted group selected from the group consisting of

phenyl, pyrrolyl, pyridyl, benzimidazolyl, naphthyl and



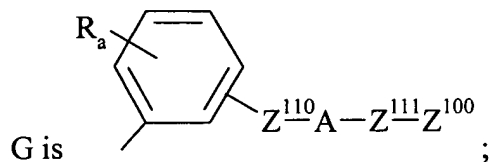
where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, Cl, Br, NO_2 , amino, N-alkylamino, N,N-dialkylamino, CN, optionally substituted alkyl, -O-(optionally substituted alkyl) and phenyl;

Z^{110} and Z^{111} for each occurrence is independently (C_0 - C_3) optionally substituted with optionally substituted phenyl; and

A is -N(R)-C(O)-N(R)-, -N(R)-S(O)₂-, -N(R)-C(O)-, -N(R)- or -N(R)-C(O)-O-.

80. A compound according to Claim 79, wherein R_a is methyl and there is only one R_a and it is F.

81. A compound according to Claim 9 or 66, wherein



Z^{100} is an optionally substituted group selected from the group consisting of phenyl, isoxazolyl, tetrahydronaphthyl, furanyl, benzofuranyl, pyridyl

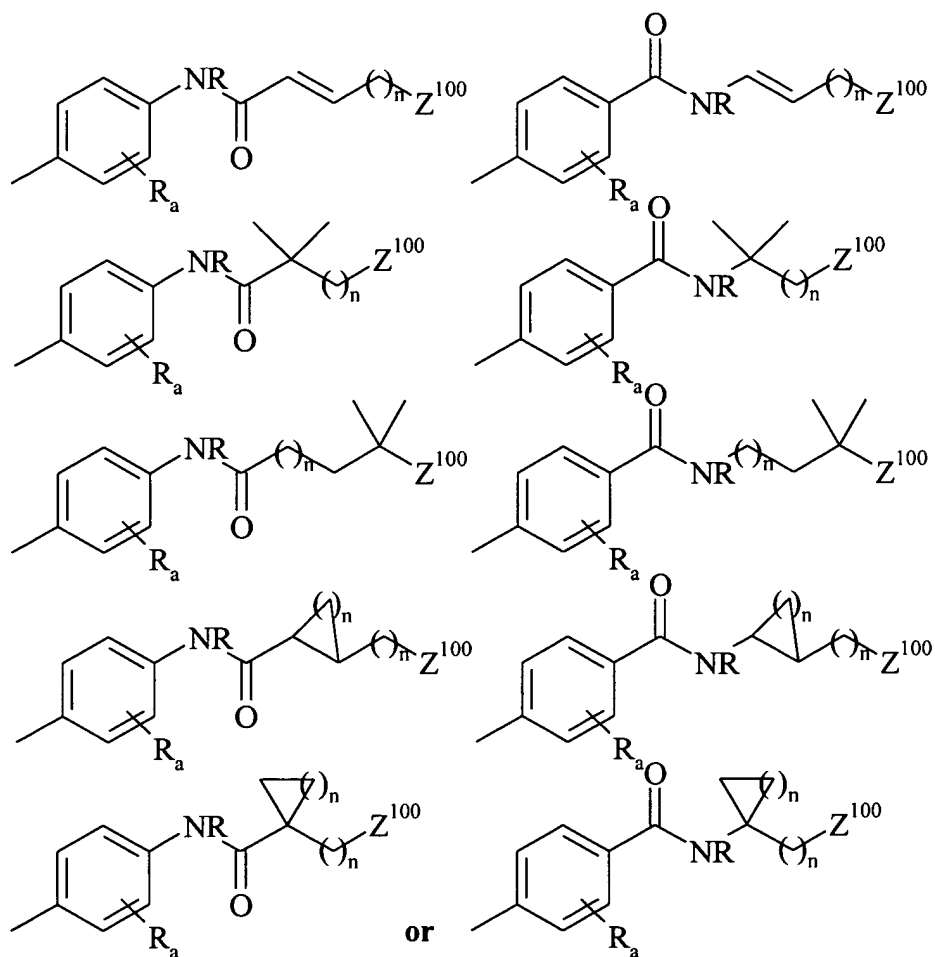
and indolyl; where Z^{100} is optionally substituted with one or more substituents each independently selected from the group consisting of F, CN, NO_2 , $-\text{C}(\text{O})\text{H}$, $-\text{CONH}_2$, $-\text{NHSO}_2\text{CF}_3$, optionally substituted alkyl, optionally substituted heteroaryl and $-\text{O}$ -(optionally substituted alkyl);

- 5 Z^{110} and Z^{111} are each independently optionally substituted ($\text{C}_0\text{-C}_3$); and
A is O, $-\text{N}(\text{R})-\text{C}(\text{O})-(\text{CH}_2)_n-\text{N}(\text{R})-$, $-\text{C}(\text{O})-\text{N}(\text{R})-$, $-\text{N}(\text{R})-\text{C}(\text{O})-\text{O}-$, $-\text{N}(\text{R})-\text{C}(\text{O})-$
or $-\text{N}(\text{R})-$.

- 10 82. A compound according to Claim 81, wherein R_4 is methyl; R_5 is H or methoxy;
and Z^{110} and Z^{111} are each unsubstituted.

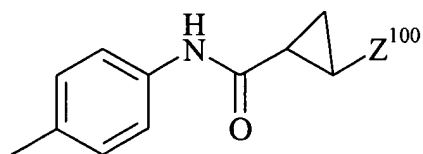
83. A compound according to Claim 9, wherein G is

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where R is H or lower alkyl and n is for each occurrence is independently 1 to 6.

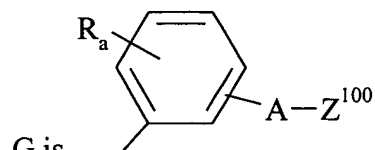
84. A compound according to Claim 83, wherein G is



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85. A compound according to Claim 84, wherein Z^{100} is substituted or unsubstituted phenyl.

86. A compound according to Claim 8, 9 or 10, wherein

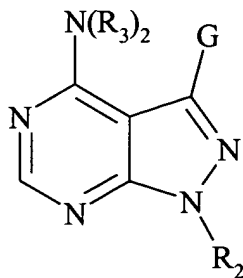


where Z^{100} is an optionally substituted group selected from the group consisting of benzoxazolyl, benzothiazolyl and benzimidazolyl.

87. A compound according to Claim 11 wherein n is 2; R_6 is H; m is 1; r is 1; and R_4 and R_5 are each hydrogen.

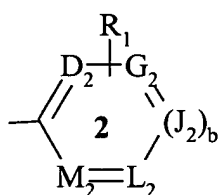
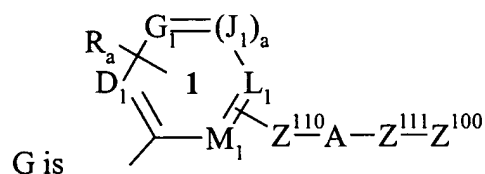
88. A compound according to claim 64 or 87 wherein G is 4-phenoxyphenyl.

89. A compound of Formula (I)



(I)

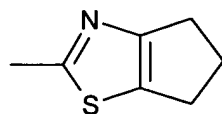
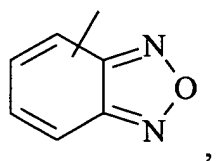
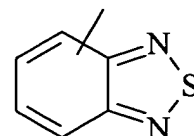
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



where Z^{100} is or a group optionally substituted with R_1 selected

from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,



, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl,

indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-

oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_l each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, $-C(O)OH$, $-C(O)H$, $-OH$, $-C(O)O$ -alkyl, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl- $S(O)_p$ -, substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl- $S(O)_p$ -, substituted or unsubstituted heteroaryl- $S(O)_p$ -, substituted or

5 unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-Z^{105}-C(O)N(R)_2$, $-Z^{105}-N(R)-C(O)-Z^{200}$, $-Z^{105}-N(R)-S(O)_2-Z^{200}$, $-Z^{105}-N(R)-C(O)-N(R)-Z^{200}$, R_c and CH_2OR_c ;

10 where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, $-CH_2-NR_dR_e$, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t-O$ -alkyl, $-W-(CH_2)_t-S$ -alkyl, or $-W-(CH_2)_t-OH$;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6) ;

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

15 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl; or R_d , R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

20 W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or NR_p , wherein R_p for each occurrence is independently H or alkyl; or

R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

25 R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

A is $-(C_1-C_6)-$, $-O-$, $-S-$, $-S(O)_p-$, $-N(R)-$, $-N(C(O)OR)-$, $-N(C(O)R)-$, $-N(SO_2R)-$,
 $-CH_2O-$, $-CH_2S-$, $-CH_2N(R)-$, $-CH(NR)-$, $-CH_2N(C(O)R)-$,
 $CH_2N(C(O)OR)-$, $-CH_2N(SO_2R)-$, $-CH(NHR)-$, $-CH(NHC(O)R)-$,
 $CH(NHSO_2R)-$, $-CH(NHC(O)OR)-$, $-CH(OC(O)R)-$, $-CH(OC(O)NHR)-$,
5 $-CH=CH-$, $-C(=NOR)-$, $-C(O)-$, $-CH(OR)-$, $-C(O)N(R)-$, $-N(R)C(O)-$,
 $-N(R)S(O)_p-$, $-OC(O)N(R)-$, $-N(R)-C(O)-(CH_2)_n-N(R)-$, $-N(R)C(O)O-$,
 $-N(R)-(CH_2)_{n+1}-C(O)-$, $-S(O)_pN(R)-$, $-O-(CR_2)_{n+1}-C(O)-$, $-O-(CR_2)_{n+1}-O-$,
 $-N(C(O)R)S(O)_p-$, $-N(R)S(O)_pN(R)-$, $-N(R)-C(O)-(CH_2)_n-O-$,
 $-C(O)N(R)C(O)-$, $-S(O)_pN(R)C(O)-$, $-OS(O)_pN(R)-$, $-N(R)S(O)_pO-$,
10 $-N(R)S(O)_pC(O)-$, $-SO_pN(C(O)R)-$, $-N(R)SO_pN(R)-$, $-C(O)O-$,
 $-N(R)P(OR_b)O-$, $-N(R)P(OR_b)-$, $-N(R)P(O)(OR_b)O-$, $-N(R)P(O)(OR_b)-$,
 $-N(C(O)R)P(OR_b)O-$, $-N(C(O)R)P(OR_b)-$, $-N(C(O)R)P(O)(OR_b)O-$, or
 $-N(C(O)R)P(OR_b)-$;

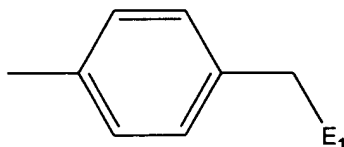
where R for each occurrence is independently H, substituted or unsubstituted alkyl,
15 substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_b for each occurrence is independently H, substituted or unsubstituted alkyl,
substituted or unsubstituted arylalkyl, substituted or unsubstituted
cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

20 in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R
and R_b together form a five- or six-membered heterocyclic ring; or
A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or
unsubstituted five or six-membered heterocyclic ring fused to ring 1; or
 $Z^{110}-A-Z^{111}$ taken together is a covalent bond; and
25 R_2 is a) hydrogen; b) substituted or unsubstituted trityl; c) substituted or
unsubstituted cycloalkenyl; d) azaheteroaryl substituted with a

substituted or unsubstituted alkyl; e) azacycloalkyl which is substituted with one or more substituents selected from substituted or unsubstituted $-(C_1-C_6)\text{-alkyl}$, substituted or unsubstituted $-C_1-C_6\text{-alkyl-OR}$, substituted or unsubstituted $-C(O)-C_1-C_6\text{-alkyl-N(R)}_2$, substituted or unsubstituted $-C_1-C_6\text{-alkyl-N(R)}_2$, substituted or unsubstituted $-C_1-C_6\text{-alkyl-cycloalkyl}$, substituted or unsubstituted tetrahydrothienyl, and substituted or unsubstituted tetrahydrothiopyranyl; or f) a group of the formula



wherein E_1 is piperidinyl, piperazinyl, imidazolyl, morpholinyl, pyrrolidinyl, amino, amido, or tetrahydrothiazolyl, and wherein E is optionally substituted with one or more substituents selected from $-C_0-C_6\text{-alkyl-OR}$, $-C_1-C_6\text{-alkyl-C(O)OR}$, $-C_1-C_6\text{-alkyl-heteroaryl}$, $-C_1-C_6\text{-alkyl-heterocycloalkyl}$, and $-C_1-C_6\text{-alkyl-N(R)}_2$;

a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group consisting of CR_a and N , provided that at least two of D_1 , G_1 , J_1 , L_1 and M_1 are CR_a ; or

a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N , wherein R_a is as defined above;

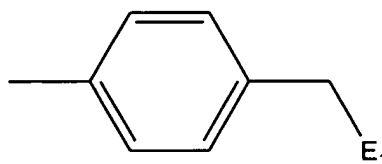
b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N , provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or

b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of

CR_n and N , wherein R_n is as defined above; and
 n for each occurrence is independently an integer from 0 to 6;
 provided that when Z^{110} -A- Z^{111} taken together are a covalent bond, then Z^{100} is
 not alkyl; and

- 5 provided that when Z^{110} -A- Z^{111} taken together are a C_1 - C_6 alkyl, then Z^{100} is not
 phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl,
 pyrazinyl, pyridazinyl, furyl or thienyl.

- 10 90. The compound of Claim 89, wherein R_2 is a group represented by the following
 structural formula:



wherein:

- 15 E_1 is selected from the group consisting of -amino- C_1 - C_6 -alkyl-morpholino, -
 piperidino-(C_1 - C_6 -alkyl-OR), -imidazolyl- C_1 - C_6 -alkyl-C(O)OR, -
 piperazino- C_1 - C_6 -alkyl-OR, -amino- C_1 - C_6 -alkyl-OR, -pyrrolidino-OR, -
 amino- C_1 - C_6 -alkyl-imidazo, -amino- C_1 - C_6 -alkyl- $N(R)_2$, -amido- C_1 - C_6 -
 alkyl- $N(R)_2$, tetrahydrothiazolyl, N,N -di-(hydroxy- C_1 - C_6 -alkyl)amino-,
 and -piperizino-OR.

- 20 91. The compound of Claim 90, wherein:

E_1 is selected from the group consisting of 4-(2-hydroxyethyl)morpholino, 3-
 hydroxymethylpiperidino, 2-[3-(methylcarboxy)propyl]imidizol-4-yl, 4-
 (2-hydroxyethyl)piperazino, 2-hydroxyethylamino, 3-
 hydroxypyrrolidino, 3-imidazolopropylamino, 4-hydroxybutylamino, 3-

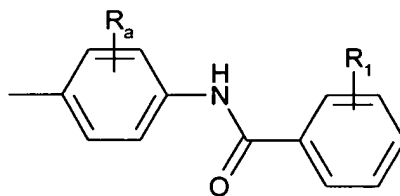
methoxypropylamino, 3-(N,N-dimethylamino)propylamino, N-[2-(N,N-dimethyl)ethyl]amido, tetrahydrothiazolyl, N,N-di-(2-hydroxyethyl)amino, 4-hydroxypiperizino, and 4-hydroxymethylpiperizino.

5

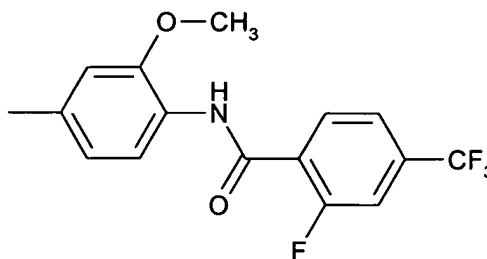
92. The compound of Claim 90, wherein Z^{110} -A- Z^{111} is $-NHC(O)-$.

93. The compound of Claim 90, wherein G is a group represented by the following structural formula:

10



94. The compound of Claim 93, wherein G is represented by the following structural formula:



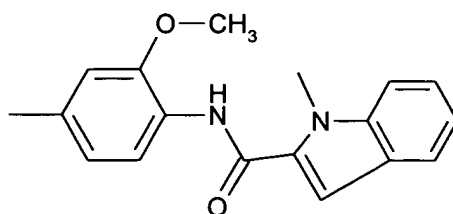
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95. The compound of Claim 89, wherein R_2 is an azaheteroaryl substituted with a C_1 - C_6 alkyl, wherein the alkyl is optionally substituted with one or more substituents selected from $RO-$, $-C(O)OR$, $-C(O)N(R)_2$, and $-N(R)_2$.

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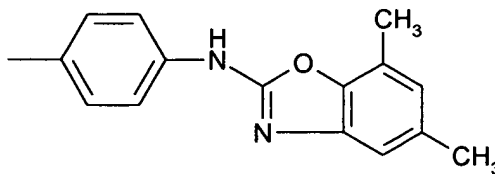
96. The compound of Claim 95, wherein R_2 is 4-(2-hydroxyethyl)pyridin-2-yl, 3-aminomethylpyridin-4-yl or 2-methylimidazol-4-yl.

5 97. The compound of Claim 96, wherein G is represented by the following formula:



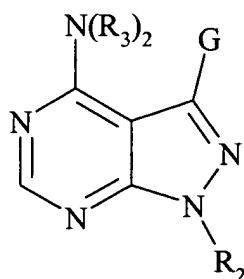
10 98. The compound of Claim 89, wherein R_2 is a pyrrolidinyl which is substituted with 2-methoxyethyl, N,N-dimethylaminomethyl, N,N-dimethylamino-1-oxoethyl, or 2-(N-methylamino)-1-oxopropyl.

99. The compound of Claim 98 wherein G is represented by the following structural formula:



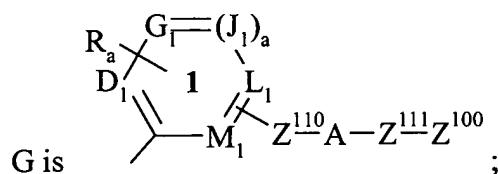
100. The compound of Claim 89, wherein R_2 is a piperidinyl which is substituted with a tetrahydrothiopyranyl, tetrahydrothienyl, 2-(N-methylamino)-2-methyl-1-oxopropyl, 2-methoxyethyl, or cyclopropylmethyl.

101. A compound of Formula (I)



(I)

racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



wherein Z^{100} is pyrrolidinyl, quinolinyl, quinoxaliny, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, H-pyridinone, 1,1-dioxybenzothiazolyl, benzoisoxazolyl, alkyl, imidazo[1,2-a]pyridinyl,

pyrrolopyridinyl or , wherein all of the foregoing Z^{100} groups are optionally substituted with R_1 ;

Z^{110} is a covalent bond, or an optionally substituted (C_1 - C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , $COOH$, substituted or

unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1 - C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_l each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, $-C(O)OH$, $-C(O)H$, $-OH$, $-C(O)O$ -alkyl, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl- $S(O)_p$ -, substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl- $S(O)_p$ -, substituted or unsubstituted heteroaryl- $S(O)_p$ -, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-Z^{105}$ -

$C(O)N(R)_2$, $-Z^{105}-N(R)-C(O)-Z^{200}$, $-Z^{105}-N(R)-S(O)_2-Z^{200}$, $-Z^{105}-N(R)-C(O)-N(R)-Z^{200}$, R_c and CH_2OR_c ;

where R_c for each occurrence is independently hydrogen, substituted or

unsubstituted alkyl, substituted or unsubstituted aryl, $-CH_2-NR_dR_e$, $-W-$

5 $(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t-O$ -alkyl, $-W-(CH_2)_t-S$ -alkyl, or $-W-(CH_2)_t-OH$;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6) ;

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

10 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl; or R_d , R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or

15 NR_p , wherein R_p for each occurrence is independently H or alkyl; or

R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a

20 substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

A is $-(C_1-C_6)-$, $-O-$, $-S-$, $-S(O)_p-$, $-N(R)-$, $-N(C(O)OR)-$, $-N(C(O)R)-$, $-N(SO_2R)-$, $-CH_2O-$, $-CH_2S-$, $-CH_2N(R)-$, $-CH(NR)-$, $-CH_2N(C(O)R)-$, $-CH_2N(C(O)OR)-$, $-CH_2N(SO_2R)-$, $-CH(NHR)-$, $-CH(NHC(O)R)-$, $-CH(NHSO_2R)-$, $-CH(NHC(O)OR)-$, $-CH(OC(O)R)-$, $-CH(OC(O)NHR)-$, $-CH=CH-$, $-C(=NOR)-$, $-C(O)-$, $-CH(OR)-$, $-C(O)N(R)-$, $-N(R)C(O)-$, $-$

25

$N(R)S(O)_p-$; $-OC(O)N(R)-$; ; $-N(R)-C(O)-(CH_2)_n-N(R)-$, $-N(R)C(O)O-$; -
 $N(R)-(CH_2)_{n+1}-C(O)-$, $-S(O)_pN(R)-$; $-O-(CR_2)_{n+1}-C(O)-$, $-O-(CR_2)_{n+1}-O-$, -
 $N(C(O)R)S(O)_p-$; $-N(R)S(O)_pN(R)-$; $-N(R)-C(O)-(CH_2)_n-O-$, -
 $C(O)N(R)C(O)-$; $-S(O)_pN(R)C(O)-$; $-OS(O)_pN(R)-$; $-N(R)S(O)_pO-$; -
5 $N(R)S(O)_pC(O)-$; $-SO_pN(C(O)R)-$; $-N(R)SO_pN(R)-$; $-C(O)O-$; -
 $N(R)P(OR_b)O-$; $-N(R)P(OR_b)-$; $-N(R)P(O)(OR_b)O-$; $-N(R)P(O)(OR_b)-$; -
 $N(C(O)R)P(OR_b)O-$; $-N(C(O)R)P(OR_b)-$; $-N(C(O)R)P(O)(OR_b)O-$, or -
 $N(C(O)R)P(OR_b)-$;

where R for each occurrence is independently H, substituted or unsubstituted alkyl,
 10 substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_b for each occurrence is independently H, substituted or unsubstituted alkyl,
 substituted or unsubstituted arylalkyl, substituted or unsubstituted
 cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

15 in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R
 and R_b together form a five- or six-membered heterocyclic ring; or
 A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or
 unsubstituted five or-six-membered heterocyclic ring fused to ring 1; or

$Z^{110}-A-Z^{111}$ taken together is a covalent bond; and

20 R_2 is H or a group of the formula $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-$
 $C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted
 or unsubstituted phenyl group;

25 Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or
 unsubstituted cycloalkyl group; a substituted or unsubstituted
 cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated

heterocyclic group; or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, nitro, halo, substituted or unsubstituted (C_1-C_6), substituted or unsubstituted aryl, substituted or unsubstituted $-C(O)$ -alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-N((C_1-C_6)-OR)_2$, substituted or unsubstituted $-N(R)-(C_1-C_6)-C(O)_2R$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted $-(C_1-C_6)-C(O)N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido, substituted or unsubstituted amino, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, oxo, and a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more heteroatoms selected from the group consisting of N, O, and S; wherein the nitrogen atoms of said heterocyclic group or heterobicyclic group are independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl; or

R_2 is a group of the formula -B-E, wherein B is a substituted or unsubstituted

cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, a substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted (C₁-C₆)-azacycloalkyl-, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-, substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-, substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino, substituted or unsubstituted arylcarbonylamino, substituted or unsubstituted

alkylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1 , G_1 , J_1 , L_1 and M_1 are CR_a ; or

5 a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or

10 b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6;

15 provided that when A is $-N(R)-$, Z^{110} and Z^{111} are each a covalent bond, and R_2 is a 3,4-dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, then Z^{100} is not alkyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl or pyrrolidinyl;

provided that when Z^{110} and Z^{111} are each a covalent bond, and R_2 is a 3,4-

20 dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, Z^{100} is a substituted or unsubstituted alkyl, then A is not alkyl, $-O-$, $-C(O)-$, $-NHC(O)-$ or $-C(O)O-$;

provided that when $Z^{110}-A-Z^{111}$ taken together are a covalent bond, then Z^{100} is not alkyl;

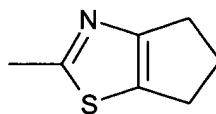
25 provided that when $Z^{110}-A-Z^{111}$ taken together are a C_1-C_6 alkyl, then Z^{100} is not phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl,

pyrazinyl, pyridazinyl, furyl or thienyl; and
 provided that when R_2 is a substituted or unsubstituted cyclopentyl, Z^{100} is an
 substituted or unsubstituted alkyl, Z^{110} and Z^{111} are each a covalent bond,
 then A is not $-O-$, $-C(O)O-$, or $-N(R)-$.

5

102. The compound of Claim 101, wherein Z^{100} is 2-pyrrolidinyl, 1,2-dihydro-2-oxopyridin-3-yl, benzoisoxazol-3-yl, 1,1-dioxybenzoisothiazol-3-yl,

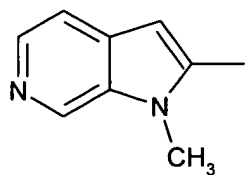
imidazo[1,2-a]pyridin-2-yl or
 methylpiperazino)-cyclohexyl.



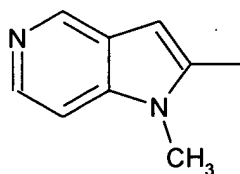
and R_2 is 4-(4-

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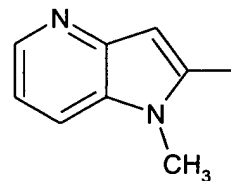
103. The compound of Claim 102, wherein Z^{110} -A- Z^{111} is $-NH-$.
104. The compound of Claim 101, wherein Z^{100} is a pyrrolopyridinyl selected from



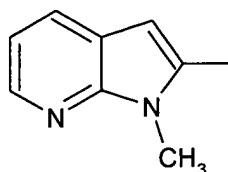
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or

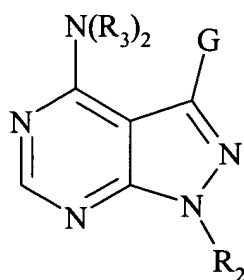


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105. The compound of Claim 104, wherein Z^{110} -A- Z^{111} is $-NHC(O)-$.

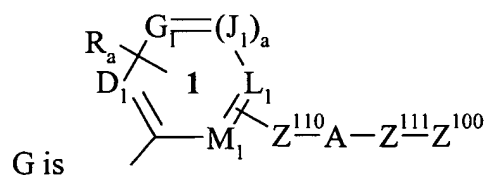
106. The compound of Claim 105, wherein R_2 is piperidin-4-yl, N-methylpiperidin-4-yl, N-(prop-2-yl)piperidin-4-yl, N-(imidazol-4-yl-methyl)piperidin-4-yl, N-(2-methylimidazol-4-yl-methyl)piperidin-4-yl, N-(pyrazol-4-yl-methyl)piperidin-4-yl, N-(2-methoxyethyl)piperidin-4-yl, N-(fur-3-yl-methyl)piperidin-4-yl, N-(tetrahydropyran-4-yl-methyl)piperidin-4-yl, N-(pyrrol-2-yl-methyl)piperidin-4-yl, or N-(2-difluoroethyl)piperidin-4-yl.

107. A compound of Formula (I)

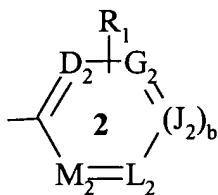


(I)

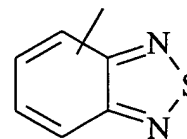
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



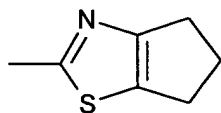
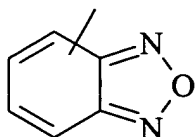
-991-



where Z^{100} is or a group optionally substituted with R_1 selected from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,



thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,



, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl,

indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , $COOH$, substituted or

unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1 - C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_i each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl- $S(O)_p$ -, substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl- $S(O)_p$ -, substituted or unsubstituted heteroaryl- $S(O)_p$ -, and wherein at least one of R_a and R_i is not hydrogen;

R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

A is $-(C_1-C_6)$ -, $-O$ -, $-S$ -, $-S(O)_p$ -, $-N(R)$ -, $-N(C(O)OR)$ -, $-N(C(O)R)$ -, $-N(SO_2R)$ -, $-CH_2O$ -, $-CH_2S$ -, $-CH_2N(R)$ -, $-CH(NR)$ -, $-CH_2N(C(O)R)$ -, $-CH_2N(C(O)OR)$ -, $-CH_2N(SO_2R)$ -, $-CH(NHR)$ -, $-CH(NHC(O)R)$ -, $-CH(NHSO_2R)$ -, $-CH(NHC(O)OR)$ -, $-CH(OC(O)R)$ -, $-CH(OC(O)NHR)$ -, $-CH=CH$ -, $-C(=NOR)$ -, $-C(O)$ -, $-CH(OR)$ -, $-C(O)N(R)$ -, $-N(R)C(O)$ -, $-N(R)S(O)_p$ -, $-OC(O)N(R)$ -, $-N(R)-C(O)-(CH_2)_n-N(R)$ -, $-N(R)C(O)O$ -,

$N(R)-(CH_2)_{n+1}-C(O)-$, $-S(O)_pN(R)-$; $-O-(CR_2)_{n+1}-C(O)-$, $-O-(CR_2)_{n+1}-O-$, $-$
 $N(C(O)R)S(O)_p-$; $-N(R)S(O)_pN(R)-$; $-N(R)-C(O)-(CH_2)_n-O-$, $-$
 $C(O)N(R)C(O)-$; $-S(O)_pN(R)C(O)-$; $-OS(O)_pN(R)-$; $-N(R)S(O)_pO-$; $-$
 $N(R)S(O)_pC(O)-$; $-SO_pN(C(O)R)-$; $-N(R)SO_pN(R)-$; $-C(O)O-$; $-$
 5 $N(R)P(OR_b)O-$; $-N(R)P(OR_b)-$; $-N(R)P(O)(OR_b)O-$; $-N(R)P(O)(OR_b)-$; $-$
 $N(C(O)R)P(OR_b)O-$; $-N(C(O)R)P(OR_b)-$; $-N(C(O)R)P(O)(OR_b)O-$, or $-$
 $N(C(O)R)P(OR_b)-$;

where R for each occurrence is independently H, substituted or unsubstituted alkyl,
 substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

10 R_b for each occurrence is independently H, substituted or unsubstituted alkyl,
 substituted or unsubstituted arylalkyl, substituted or unsubstituted
 cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R
 15 and R_b together form a five- or six-membered heterocyclic ring; or
 A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or
 unsubstituted five or-six-membered heterocyclic ring fused to ring 1; or
 $Z^{110}-A-Z^{111}$ taken together is a covalent bond; and

R_2 is H or a group of the formula $-Z^{101}-Z^{102}$;

20 Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-$
 $C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted
 or unsubstituted phenyl group;

25 Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or
 unsubstituted cycloalkyl group; a substituted or unsubstituted
 cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated
 heterocyclic group; or a substituted or unsubstituted, saturated or

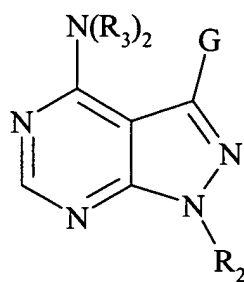
- unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl,
- 5 cyano, nitro, halo, substituted or unsubstituted (C_1-C_6), substituted or unsubstituted aryl, substituted or unsubstituted $-C(O)$ -alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-N((C_1-C_6)-OR)_2$, substituted or unsubstituted $-N(R)-(C_1-C_6)-C(O)_2R$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted $-(C_1-C_6)-C(O)N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido, substituted or unsubstituted amino, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, oxo, and a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more heteroatoms selected from the group consisting of N, O, and S; wherein the nitrogen atoms of said heterocyclic group or heterobicyclic group are
- 10 independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl; or
- 15 20 25 R_2 is a group of the formula $-B-E$, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted

heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, a substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted (C₁-C₆)-azacycloalkyl-, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-, substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-, substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino, substituted or unsubstituted arylcarbonylamino, substituted or unsubstituted alkylcarbonylamino or substituted or unsubstituted aryl;

- a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1 , G_1 , J_1 , L_1 and M_1 are CR_a ; or
- 5 a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;
- b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or
- 10 b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and
- n for each occurrence is independently an integer from 0 to 6;
- provided that when A is $-N(R)-$, Z^{110} and Z^{111} are each a covalent bond, and R_2 is
- 15 a 3,4-dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, then Z^{100} is not alkyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl or pyrrolidinyl;
- provided that when Z^{110} and Z^{111} are each a covalent bond, and R_2 is a 3,4-dihydroxytetrahydrofur-2-yl or a 3,4-diacyloxytetrahydrofur-2-yl, Z^{100} is
- 20 a substituted or unsubstituted alkyl, then A is not alkyl, $-O-$, $-C(O)-$, $-NHC(O)-$ or $-C(O)O-$;
- provided that when $Z^{110}-A-Z^{111}$ taken together are a covalent bond, then Z^{100} is not alkyl;
- provided that when $Z^{110}-A-Z^{111}$ taken together are a C_1-C_6 alkyl, then Z^{100} is not
- 25 phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, furyl or thienyl; and

provided that when R_2 is a substituted or unsubstituted cyclopentyl, Z^{100} is an substituted or unsubstituted alkyl, Z^{110} and Z^{111} are each a covalent bond, then A is not $-O-$, $-C(O)O-$, or $-N(R)-$.

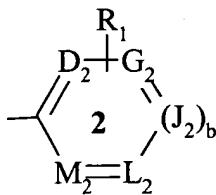
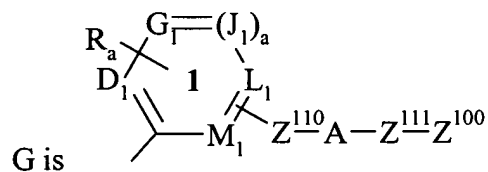
5 108. A compound of Formula (I)



(I)

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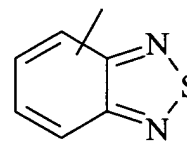
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



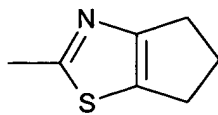
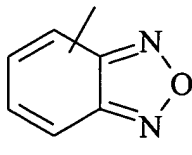
15

where Z^{100} is or a group optionally substituted with R_1 selected from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl,

quinoxaliny, quinazoliny, isoquinoliny, phthalaziny, imidazo[1,2-a]pyrimidiny, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,



thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,



, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl,

indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indoliny, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , $COOH$, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , $COOH$,

substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_i each represent one or more substituents for each occurrence

independently selected from the group consisting of hydrogen, halogen, -
 5 CN, $-\text{NO}_2$, $-\text{C}(\text{O})\text{OH}$, $-\text{C}(\text{O})\text{H}$, $-\text{OH}$, $-\text{C}(\text{O})\text{O-alkyl}$, $-\text{C}(\text{O})\text{O-aryl}$, $-\text{C}(\text{O})\text{O-heteroaryl}$, $-\text{C}(\text{O})\text{-alkyl}$, $-\text{C}(\text{O})\text{-aryl}$, $-\text{C}(\text{O})\text{-heteroaryl}$, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted
 10 alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl- $\text{S}(\text{O})_p$ -,
 15 substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl- $\text{S}(\text{O})_p$ -, substituted or unsubstituted heteroaryl- $\text{S}(\text{O})_p$ -, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-\text{Z}^{105}$ -
 20 $\text{C}(\text{O})\text{N}(\text{R})_2$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-C}(\text{O})\text{-Z}^{200}$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-S}(\text{O})_2\text{-Z}^{200}$, $-\text{Z}^{105}\text{-N}(\text{R})\text{-C}(\text{O})\text{-N}(\text{R})\text{-Z}^{200}$, R_c and CH_2OR_c ;

where R_c for each occurrence is independently hydrogen, substituted or

25 unsubstituted alkyl, substituted or unsubstituted aryl, $-\text{CH}_2\text{-NR}_d\text{R}_e$, $-\text{W-}(\text{CH}_2)_i\text{-NR}_d\text{R}_e$, $-\text{W-}(\text{CH}_2)_i\text{-O-alkyl}$, $-\text{W-}(\text{CH}_2)_i\text{-S-alkyl}$, or $-\text{W-}(\text{CH}_2)_i\text{-OH}$;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6) ;

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

5 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl; or R_d , R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or

10 NR_p , wherein R_f for each occurrence is independently H or alkyl; or

R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a

15 substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

A is $-(C_1-C_6)-$;

R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

20 p is 1 or 2;

R_2 is H or a group of the formula $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;

25 Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or unsubstituted cycloalkyl group; a substituted or unsubstituted

cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated
 heterocyclic group; or a substituted or unsubstituted, saturated or
 unsaturated heterobicyclic group; wherein said substituted alkyl,
 substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic
 5 and substituted heterobicyclic group having one or more substituents
 each independently selected from the group consisting of hydroxyl,
 cyano, nitro, halo, substituted or unsubstituted (C_1-C_6), substituted or
 unsubstituted aryl, substituted or unsubstituted $-C(O)$ -alkyl, substituted
 or unsubstituted alkoxy, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$,
 10 substituted or unsubstituted $-N((C_1-C_6)-OR)_2$, substituted or
 unsubstituted $-N(R)-(C_1-C_6)-C(O)_2R$, substituted or unsubstituted $-(C_1-$
 $C_6)-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-$
 $C_6)-N(R)_2$, substituted or unsubstituted $-(C_1-C_6)-C(O)N(R)-(C_1-C_6)-$
 $N(R)_2$, substituted or unsubstituted sulfonamido, substituted or
 15 unsubstituted ureido, substituted or unsubstituted carboxamido,
 substituted or unsubstituted amino, substituted or unsubstituted $-N(R)-$
 $(C_1-C_6)-OR$, oxo, and a saturated, unsaturated or aromatic, substituted or
 unsubstituted heterocyclic group comprising one or more heteroatoms
 selected from the group consisting of N, O, and S; wherein the nitrogen
 20 atoms of said heterocyclic group or heterobicyclic group are
 independently optionally substituted by oxo, substituted or unsubstituted
 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or
 unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)-$
 25 heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or
 unsubstituted heteroarylalkyl; or

R_2 is a group of the formula -B-E, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, a substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted (C_1-C_6) -azacycloalkyl-, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-, substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-, substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino, substituted or

unsubstituted arylcarbonylamino, substituted or unsubstituted
alkylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group
consisting of CR_a and N, provided that at least two of D_1 , G_1 , J_1 , L_1 and
5 M_1 are CR_a ; or

a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and
the remainder are independently selected from the group consisting of
 CR_a and N, wherein R_a is as defined above;

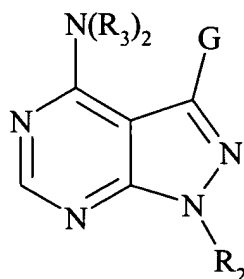
b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group
consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and
10 M_2 are CR_a ; or

b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and
the remainder are independently selected from the group consisting of
 CR_a and N, wherein R_a is as defined above; and

15 n for each occurrence is independently an integer from 0 to 6;
provided that when Z^{110} -A- Z^{111} taken together are a C_1 - C_6 alkyl, then Z^{100} is not
phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, pyridazinyl, furyl or thienyl.

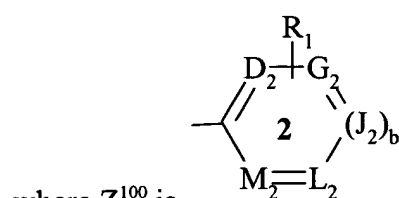
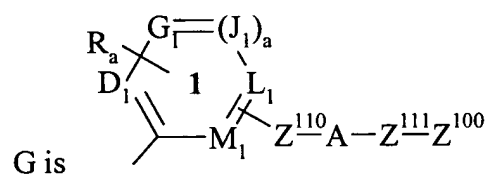
20 109. A compound of Formula (I)

-1004-



(I)

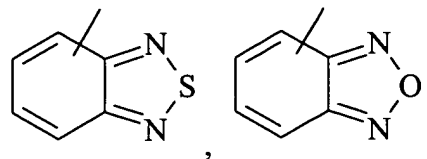
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:

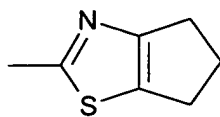


or a group optionally substituted with R_1 selected

from the group consisting of pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl, thienyl, benzoxazolyl,

benzoxisoxazolyl, benzothiazolyl,





5 , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

R_a and R_i each represent one or more substituents for each occurrence

10 independently selected from the group consisting of hydrogen, halogen, -CN, -NO₂, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)-alkyl, -C(O)-aryl, -C(O)-heteroaryl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl-S(O)_p-, substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-S(O)_p-, substituted or unsubstituted heteroaryl-S(O)_p-, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or

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25

unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-Z^{105}-C(O)N(R)_2$, $-Z^{105}-N(R)-C(O)-Z^{200}$, $-Z^{105}-N(R)-S(O)_2-Z^{200}$, $-Z^{105}-N(R)-C(O)-N(R)-Z^{200}$, R_c and CH_2OR_c ;

where R_c for each occurrence is independently hydrogen, substituted or

5 unsubstituted alkyl, substituted or unsubstituted aryl, $-CH_2-NR_dR_e$, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t-O$ -alkyl, $-W-(CH_2)_t-S$ -alkyl, or $-W-(CH_2)_t-OH$;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6) ;

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6) ,
10 substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl;
or R_d , R_e and the nitrogen atom to which they are attached together form
a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

15 W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or NR_f , wherein R_f for each occurrence is independently H or alkyl; or
 R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with
ring 2;

R_3 for each occurrence is, independently, hydrogen, hydroxy, substituted or
20 unsubstituted alkyl, substituted or unsubstituted $-C(O)$ -alkyl, a
substituted or unsubstituted $-C(O)$ -aryl, or a substituted or unsubstituted
 $-C(O)$ -heteroaryl or substituted or unsubstituted alkoxy;

R for each occurrence is independently H, substituted or unsubstituted alkyl,
substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

25 p is 1 or 2;

$Z^{110}-A-Z^{111}$ taken together is a covalent bond; and

R_2 is H or a group of the formula $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;

- 5 Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or unsubstituted cycloalkyl group; a substituted or unsubstituted cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated heterocyclic group; or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, nitro, halo, substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted aryl, substituted or unsubstituted $-C(O)-$ alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-N((C_1-C_6)-OR)_2$, substituted or unsubstituted $-N(R)-(C_1-C_6)-C(O)_2R$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted $-(C_1-C_6)-C(O)N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido, substituted or unsubstituted amino, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, oxo, and a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more heteroatoms selected from the group consisting of N, O, and S; wherein the nitrogen atoms of said heterocyclic group or heterobicyclic group are
- 10
- 15
- 20
- 25

independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl; or

R_2 is a group of the formula $-B-E$, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted or unsubstituted azacycloalkyl, a substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted (C_1-C_6) -azacycloalkyl-, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl- $N(R)-(C_1-C_6)-$, substituted or unsubstituted aryl- $N(R)-(C_1-C_6)-$, substituted or unsubstituted alkyl- $N(R)-(C_1-C_6)-$, substituted or unsubstituted heteroaryl- $(C_1-C_6)-N(R)-$, substituted or unsubstituted aryl- $(C_1-C_6)-N(R)-$, substituted or unsubstituted alkyl- $(C_1-C_6)-N(R)-$, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl,

substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino, substituted or unsubstituted arylcarbonylamino, substituted or unsubstituted alkylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1 , G_1 , J_1 , L_1 and M_1 are CR_a ; or

a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

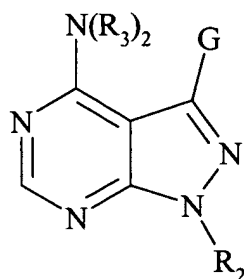
b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or

b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.

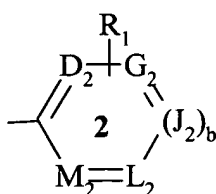
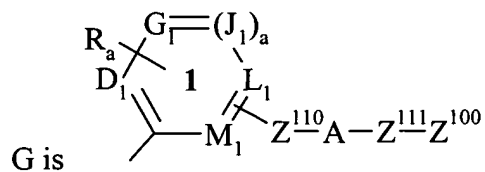
110. A compound of Formula (I)

-1010-



(I)

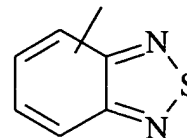
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:



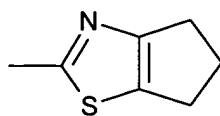
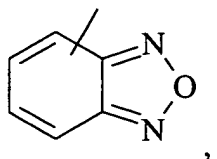
where Z^{100} is or a group optionally substituted with R_1 selected

from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxaliny, quinazoliny, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,



,



5 , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-

10 Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

15 Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

20 R_a and R_i each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, $-C(O)OH$, $-C(O)H$, $-OH$, $-C(O)O$ -alkyl, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted

or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino,
 trifluoromethylsulfonamido, substituted or unsubstituted alkyl,
 substituted or unsubstituted cycloalkyl, substituted or unsubstituted
 alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted
 5 heteroaryl, substituted or unsubstituted alkenyl, substituted or
 unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy,
 substituted or unsubstituted heteroarylalkoxy, substituted or
 unsubstituted arylalkoxy, substituted or unsubstituted alkyl-S(O)_p-,
 substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-
 10 S(O)_p-, substituted or unsubstituted heteroaryl-S(O)_p-, substituted or
 unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl,
 substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
 alkynyl, substituted or unsubstituted amino, substituted or unsubstituted
 aminoalkyl, substituted or unsubstituted amido groups, substituted or
 15 unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z¹⁰⁵-
 C(O)N(R)₂, -Z¹⁰⁵-N(R)-C(O)-Z²⁰⁰, -Z¹⁰⁵-N(R)-S(O)₂-Z²⁰⁰, -Z¹⁰⁵-N(R)-
 C(O)-N(R)-Z²⁰⁰, R_c and CH₂OR_c;

where R_c for each occurrence is independently hydrogen, substituted or
 unsubstituted alkyl, substituted or unsubstituted aryl, -CH₂-NR_dR_e, -W-
 20 (CH₂)_i-NR_dR_e, -W-(CH₂)_i-O-alkyl, -W-(CH₂)_i-S-alkyl, or -W-(CH₂)_i-OH;
 Z¹⁰⁵ for each occurrence is independently a covalent bond or (C₁-C₆);
 Z²⁰⁰ for each occurrence is independently a substituted or unsubstituted (C₁-C₆),
 substituted or unsubstituted phenyl or substituted or unsubstituted -(C₁-
 C₆)-phenyl;
 25 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO₂-alkyl;
 or R_d, R_e and the nitrogen atom to which they are attached together form

a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, S(O), S(O)₂, or

NR_f, wherein R_f for each occurrence is independently H or alkyl; or

5 R₁ is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R₃ for each occurrence is, independently, substituted or unsubstituted -C(O)-alkyl, a substituted or unsubstituted -C(O)-aryl, or a substituted or unsubstituted -C(O)-heteroaryl.

10 A is -(C₁-C₆)-, -O-, -S-, -S(O)_p-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -N(SO₂R)-; -CH₂O-; -CH₂S-; -CH₂N(R)-; -CH(NR)-; -CH₂N(C(O)R)-; -CH₂N(C(O)OR)-; -CH₂N(SO₂R)-; -CH(NHR)-; -CH(NHC(O)R)-; -CH(NHSO₂R)-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR)-; -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -N(R)S(O)_p-; -OC(O)N(R)-; -N(R)-C(O)-(CH₂)_n-N(R)-, -N(R)C(O)O-; -N(R)-(CH₂)_{n+1}-C(O)-, -S(O)_pN(R)-; -O-(CR₂)_{n+1}-C(O)-, -O-(CR₂)_{n+1}-O-, -N(C(O)R)S(O)_p-; -N(R)S(O)_pN(R)-; -N(R)-C(O)-(CH₂)_n-O-, -C(O)N(R)C(O)-; -S(O)_pN(R)C(O)-; -OS(O)_pN(R)-; -N(R)S(O)_pO-; -N(R)S(O)_pC(O)-; -SO_pN(C(O)R)-; -N(R)SO_pN(R)-; -C(O)O-; -N(R)P(OR_b)O-; -N(R)P(OR_b)-; -N(R)P(O)(OR_b)O-; -N(R)P(O)(OR_b)-; -N(C(O)R)P(OR_b)O-; -N(C(O)R)P(OR_b)-; -N(C(O)R)P(O)(OR_b)O-, or -N(C(O)R)P(OR_b)-;

15

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where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

25 R_b for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted

cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_b together form a five- or six-membered heterocyclic ring; or

5 A is NRSO₂ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1; or

Z¹¹⁰-A-Z¹¹¹ taken together is a covalent bond; and

R₂ is H or a group of the formula -Z¹⁰¹-Z¹⁰²;

10 Z¹⁰¹ is a covalent bond, -(C₁-C₆)-, -(C₁-C₆)-O-, -(C₁-C₆)-C(O)-, -(C₁-C₆)-C(O)O-, -(C₁-C₆)-C(O)-NH-, -(C₁-C₆)-C(O)-N((C₁-C₆))- or a substituted or unsubstituted phenyl group;

15 Z¹⁰² is hydrogen; a substituted or unsubstituted alkyl group; a substituted or unsubstituted cycloalkyl group; a substituted or unsubstituted cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated heterocyclic group; or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, 20 cyano, nitro, halo, substituted or unsubstituted (C₁-C₆), substituted or unsubstituted aryl, substituted or unsubstituted -C(O)-alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted -N(R)-(C₁-C₆)-OR, substituted or unsubstituted -N((C₁-C₆)-OR)₂, substituted or unsubstituted -N(R)-(C₁-C₆)-C(O)₂R, substituted or unsubstituted -(C₁-C₆)-N(R)-(C₁-C₆)-OR, substituted or unsubstituted -(C₁-C₆)-N(R)₂, substituted or unsubstituted -(C₁-C₆)-C(O)N(R)-(C₁-C₆)-

25

- N(R)₂, substituted or unsubstituted sulfonamido, substituted or
 unsubstituted ureido, substituted or unsubstituted carboxamido,
 substituted or unsubstituted amino, substituted or unsubstituted -N(R)-
 (C₁-C₆) -OR, oxo, and a saturated, unsaturated or aromatic, substituted or
 5 unsubstituted heterocyclic group comprising one or more heteroatoms
 selected from the group consisting of N, O, and S; wherein the nitrogen
 atoms of said heterocyclic group or heterobicyclic group are
 independently optionally substituted by oxo, substituted or unsubstituted
 alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 10 heteroaryl, substituted or unsubstituted -C(O)N(R)₂, substituted or
 unsubstituted -C(O)-(C₁-C₆)-N(R)₂, -C(O)-alkyl, -C(O)-aryl, -C(O)-
 heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or
 unsubstituted heteroarylalkyl; or
 R₂ is a group of the formula -B-E, wherein B is a substituted or unsubstituted
 15 cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted
 heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or
 unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl,
 substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted
 alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or
 20 unsubstituted alkylene, substituted or unsubstituted aminoalkyl,
 substituted or unsubstituted alkylencarbonyl or substituted or
 unsubstituted aminoalkylcarbonyl group; and E is substituted or
 unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted
 or unsubstituted azacycloalkyl, a substituted or unsubstituted
 25 heterocycloalkyl, substituted or unsubstituted (C₁-C₆)-azacycloalkyl-,
 substituted or unsubstituted azacycloalkylcarbonyl, substituted or

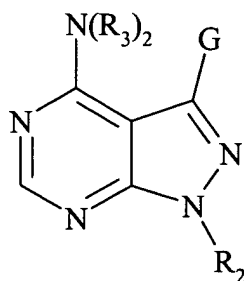
- unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted
 azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-
 , substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or
 unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted
 5 heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-
 , substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or
 unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl,
 substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted
 arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted
 10 or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl,
 substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted
 arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino,
 substituted or unsubstituted heteroarylcarbonylamino, substituted or
 unsubstituted arylcarbonylamino, substituted or unsubstituted
 15 alkylcarbonylamino or substituted or unsubstituted aryl;
 a is 1 and D₁, G₁, J₁, L₁ and M₁ are each independently selected from the group
 consisting of CR_a and N, provided that at least two of D₁, G₁, J₁, L₁ and
 M₁ are CR_a; or
 a is 0, and one of D₁, G₁, L₁ and M₁ is NR_a, one of D₁, G₁, L₁ and M₁ is CR_a and
 20 the remainder are independently selected from the group consisting of
 CR_a and N, wherein R_a is as defined above;
 b is 1 and D₂, G₂, J₂, L₂ and M₂ are each independently selected from the group
 consisting of CR_a and N, provided that at least two of D₂, G₂, J₂, L₂ and
 M₂ are CR_a; or
 25 b is 0, and one of D₂, G₂, L₂ and M₂ is NR_a, one of D₂, G₂, L₂ and M₂ is CR_a and
 the remainder are independently selected from the group consisting of

-1017-

CR_n and N, wherein R_n is as defined above; and
 n for each occurrence is independently an integer from 0 to 6;
 provided that when A is $-N(R)-$, Z^{110} and Z^{111} are each a covalent bond, and R_2 is
 a 3,4-dihydroxytetrahydrofuran-2-yl or a 3,4-diacetyloxytetrahydrofuran-2-yl,
 then Z^{100} is not alkyl, tetrahydropyranyl, tetrahydrofuran-2-yl, piperidinyl or
 pyrrolidinyl;
 provided that when Z^{110} and Z^{111} are each a covalent bond, and R_2 is a 3,4-
 dihydroxytetrahydrofuran-2-yl or a 3,4-diacetyloxytetrahydrofuran-2-yl, Z^{100} is
 a substituted or unsubstituted alkyl, then A is not alkyl, $-O-$, $-C(O)-$, $-$
 $NHC(O)-$ or $-C(O)O-$;
 provided that when $Z^{110}-A-Z^{111}$ taken together are a covalent bond, then Z^{100} is
 not alkyl;
 provided that when $Z^{110}-A-Z^{111}$ taken together are a C_1-C_6 alkyl, then Z^{100} is not
 phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl,
 pyrazinyl, pyridazinyl, furyl or thienyl; and
 provided that when R_2 is a substituted or unsubstituted cyclopentyl, Z^{100} is an
 substituted or unsubstituted alkyl, Z^{110} and Z^{111} are each a covalent bond,
 then A is not $-O-$, $-C(O)O-$, or $-N(R)-$.

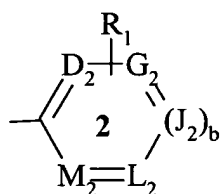
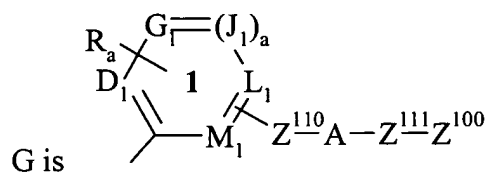
111. A compound of Formula (I)

-1018-



(I)

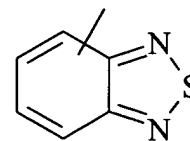
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:

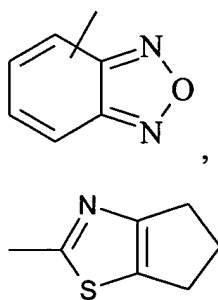


where Z^{100} is or a group optionally substituted with R_1 selected

from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,





5

, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

10

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

15

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

20

R_a and R_l each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, $-C(O)OH$, $-C(O)H$, $-OH$, $-C(O)O$ -alkyl, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted

or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino,
 trifluoromethylsulfonamido, substituted or unsubstituted alkyl,
 substituted or unsubstituted cycloalkyl, substituted or unsubstituted
 alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted
 5 heteroaryl, substituted or unsubstituted alkenyl, substituted or
 unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy,
 substituted or unsubstituted heteroarylalkoxy, substituted or
 unsubstituted arylalkoxy, substituted or unsubstituted alkyl-S(O)_p-,
 substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-
 10 S(O)_p-, substituted or unsubstituted heteroaryl-S(O)_p-, substituted or
 unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl,
 substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
 alkynyl, substituted or unsubstituted amino, substituted or unsubstituted
 aminoalkyl, substituted or unsubstituted amido groups, substituted or
 15 unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z¹⁰⁵-
 C(O)N(R)₂, -Z¹⁰⁵-N(R)-C(O)-Z²⁰⁰, -Z¹⁰⁵-N(R)-S(O)₂-Z²⁰⁰, -Z¹⁰⁵-N(R)-
 C(O)-N(R)-Z²⁰⁰, R_c and CH₂OR_c;

where R_c for each occurrence is independently hydrogen, substituted or
 unsubstituted alkyl, substituted or unsubstituted aryl, -CH₂-NR_dR_e, -W-
 20 (CH₂)_t-NR_dR_e, -W-(CH₂)_t-O-alkyl, -W-(CH₂)_t-S-alkyl, or -W-(CH₂)_t-OH;
 Z¹⁰⁵ for each occurrence is independently a covalent bond or (C₁-C₆);
 Z²⁰⁰ for each occurrence is independently a substituted or unsubstituted (C₁-C₆),
 substituted or unsubstituted phenyl or substituted or unsubstituted -(C₁-
 C₆)-phenyl;
 25 R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO₂-alkyl;
 or R_d, R_e and the nitrogen atom to which they are attached together form

a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, S(O), S(O)₂, or

NR_f, wherein R_f for each occurrence is independently H or alkyl; or

5 R₁ is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R₃ for each occurrence is, independently, hydrogen, hydroxy, substituted or

unsubstituted alkyl, substituted or unsubstituted -C(O)-alkyl, a

substituted or unsubstituted -C(O)-aryl, or a substituted or unsubstituted

10 -C(O)-heteroaryl or substituted or unsubstituted alkoxy;

A is -(C₁-C₆)-, -O-, -S-, -S(O)_p-, -N(R)-, -N(C(O)OR)-, -N(C(O)R)-, -N(SO₂R)-

; -CH₂O-, -CH₂S-, -CH₂N(R)-, -CH(NR)-, -CH₂N(C(O)R)-, -

CH₂N(C(O)OR)-, -CH₂N(SO₂R)-, -CH(NHR)-, -CH(NHC(O)R)-, -

CH(NHSO₂R)-, -CH(NHC(O)OR)-, -CH(OC(O)R)-, -CH(OC(O)NHR)-;

15 -CH=CH-, -C(=NOR)-, -C(O)-, -CH(OR)-, -C(O)N(R)-, -N(R)C(O)-, -

N(R)S(O)_p-, -OC(O)N(R)-, -N(R)-C(O)-(CH₂)_n-N(R)-, -N(R)C(O)O-, -

N(R)-(CH₂)_{n+1}-C(O)-, -S(O)_pN(R)-, -O-(CR₂)_{n+1}-C(O)-, -O-(CR₂)_{n+1}-O-, -

N(C(O)R)S(O)_p-, -N(R)S(O)_pN(R)-, -N(R)-C(O)-(CH₂)_n-O-, -

C(O)N(R)C(O)-, -S(O)_pN(R)C(O)-, -OS(O)_pN(R)-, -N(R)S(O)_pO-, -

20 N(R)S(O)_pC(O)-, -SO_pN(C(O)R)-, -N(R)SO_pN(R)-, -C(O)O-, -

N(R)P(OR_b)O-, -N(R)P(OR_b)-, -N(R)P(O)(OR_b)O-, -N(R)P(O)(OR_b)-, -

N(C(O)R)P(OR_b)O-, -N(C(O)R)P(OR_b)-, -N(C(O)R)P(O)(OR_b)O-, or -

N(C(O)R)P(OR_b)-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl,

25 substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_b for each occurrence is independently H, substituted or unsubstituted alkyl,

substituted or unsubstituted arylalkyl, substituted or unsubstituted
cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R

5 and R_b together form a five- or six-membered heterocyclic ring; or

A is NRSO₂ and R, R_a and the nitrogen atom together form a substituted or

unsubstituted five or six-membered heterocyclic ring fused to ring 1; or

Z¹¹⁰-A-Z¹¹¹ taken together is a covalent bond; and

R₂ is a group of the formula -Z¹⁰¹-Z¹⁰²;

10 Z¹⁰¹ is a covalent bond, -(C₁-C₆)-, -(C₁-C₆)-O-, -(C₁-C₆)-C(O)-, -(C₁-C₆)-C(O)O-, -(C₁-C₆)-C(O)-NH-, -(C₁-C₆)-C(O)-N((C₁-C₆))- or a substituted or unsubstituted phenyl group;

Z¹⁰² is a substituted or unsubstituted cycloalkenyl, wherein said substituted

15 cycloalkenyl has one or more substituents each independently selected from the group consisting of hydroxyl, cyano, nitro, halo, substituted or unsubstituted (C₁-C₆), substituted or unsubstituted aryl, substituted or unsubstituted -C(O)-alkyl, substituted or unsubstituted alkoxy,

substituted or unsubstituted -N(R)-(C₁-C₆)-OR, substituted or unsubstituted -N((C₁-C₆)-OR)₂, substituted or unsubstituted -N(R)-(C₁-C₆)-C(O)₂R, substituted or unsubstituted -(C₁-C₆)-N(R)-(C₁-C₆)-OR, substituted or unsubstituted -(C₁-C₆)-N(R)-(C₁-C₆)-N(R)₂, substituted or unsubstituted -(C₁-C₆)-C(O)N(R)-(C₁-C₆)-N(R)₂, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido, substituted or unsubstituted amino, substituted or unsubstituted -N(R)-(C₁-C₆)-OR, oxo, and a saturated, unsaturated or aromatic, substituted or unsubstituted

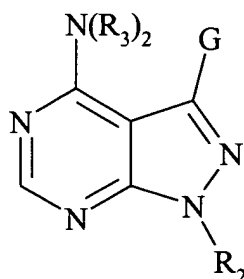
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- heterocyclic group comprising one or more heteroatoms selected from the group consisting of N, O, and S; wherein the nitrogen atoms of said heterocyclic group or heterobicyclic group are independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl;
- 5
- 10 a is 1 and D_1 , G_1 , J_1 , L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1 , G_1 , J_1 , L_1 and M_1 are CR_a ; or
- a is 0, and one of D_1 , G_1 , L_1 and M_1 is NR_a , one of D_1 , G_1 , L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of
- 15 CR_a and N, wherein R_a is as defined above;
- b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or
- b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and
- 20 the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and
- n for each occurrence is independently an integer from 0 to 6.

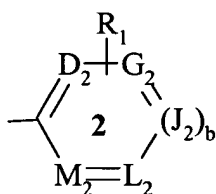
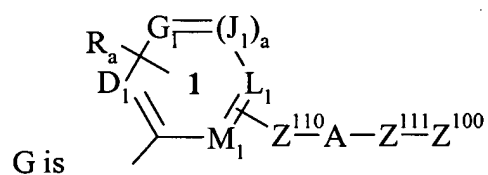
112. A compound of Formula (I)

-1024-



(I)

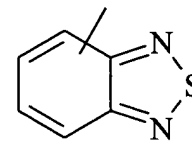
racemic-diastereomeric mixtures, optical isomers, pharmaceutically-acceptable salts, prodrugs or biologically active metabolites thereof wherein:

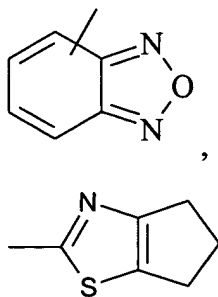


where Z^{100} is or a group optionally substituted with R_1 selected

from the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,





, thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted $-(CH_2)_n$ -cycloalkyl- $(CH_2)_n$ -; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2 , COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_i each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, $-NO_2$, $-C(O)OH$, $-C(O)H$, $-OH$, $-C(O)O$ -alkyl, $-C(O)O$ -aryl, $-C(O)O$ -heteroaryl, $-C(O)$ -alkyl, $-C(O)$ -aryl, $-C(O)$ -heteroaryl, substituted

or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino,
 trifluoromethylsulfonamido, substituted or unsubstituted alkyl,
 substituted or unsubstituted cycloalkyl, substituted or unsubstituted
 alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted
 heteroaryl, substituted or unsubstituted alkenyl, substituted or
 unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy,
 substituted or unsubstituted heteroarylalkoxy, substituted or
 unsubstituted arylalkoxy, substituted or unsubstituted alkyl-S(O)_p-,
 substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-
 S(O)_p-, substituted or unsubstituted heteroaryl-S(O)_p-, substituted or
 unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl,
 substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
 alkynyl, substituted or unsubstituted amino, substituted or unsubstituted
 aminoalkyl, substituted or unsubstituted amido groups, substituted or
 unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z¹⁰⁵-
 C(O)N(R)₂, -Z¹⁰⁵-N(R)-C(O)-Z²⁰⁰, -Z¹⁰⁵-N(R)-S(O)₂-Z²⁰⁰, -Z¹⁰⁵-N(R)-
 C(O)-N(R)-Z²⁰⁰, R_c and CH₂OR_c;

where R_c for each occurrence is independently hydrogen, substituted or
 unsubstituted alkyl, substituted or unsubstituted aryl, -CH₂-NR_dR_e, -W-
 (CH₂)_t-NR_dR_e, -W-(CH₂)_t-O-alkyl, -W-(CH₂)_t-S-alkyl, or -W-(CH₂)_t-OH;
 Z¹⁰⁵ for each occurrence is independently a covalent bond or (C₁-C₆);
 Z²⁰⁰ for each occurrence is independently a substituted or unsubstituted (C₁-C₆),
 substituted or unsubstituted phenyl or substituted or unsubstituted -(C₁-
 C₆)-phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO₂-alkyl;
 or R_d, R_e and the nitrogen atom to which they are attached together form

a five- or six-membered heterocyclic ring;

t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, S(O), S(O)₂, or

NR_p, wherein R_f for each occurrence is independently H or alkyl; or

5 R₁ is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R₃ for each occurrence is, independently, hydrogen, hydroxy, substituted or unsubstituted alkyl, substituted or unsubstituted -C(O)-alkyl, a substituted or unsubstituted -C(O)-aryl, or a substituted or unsubstituted
10 -C(O)-heteroaryl or substituted or unsubstituted alkoxy;

A is -(C₁-C₆)-, -O-, -S-, -S(O)_p-, -N(R)-, -N(C(O)OR)-, -N(C(O)R)-, -N(SO₂R)-, -CH₂O-, -CH₂S-, -CH₂N(R)-, -CH(NR)-, -CH₂N(C(O)R)-, -CH₂N(C(O)OR)-, -CH₂N(SO₂R)-, -CH(NHR)-, -CH(NHC(O)R)-, -CH(NHSO₂R)-, -CH(NHC(O)OR)-, -CH(OC(O)R)-, -CH(OC(O)NHR)-,
15 -CH=CH-, -C(=NOR)-, -C(O)-, -CH(OR)-, -C(O)N(R)-, -N(R)C(O)-, -N(R)S(O)_p-, -OC(O)N(R)-, -N(R)-C(O)-(CH₂)_n-N(R)-, -N(R)C(O)O-, -N(R)-(CH₂)_{n+1}-C(O)-, -S(O)_pN(R)-, -O-(CR₂)_{n+1}-C(O)-, -O-(CR₂)_{n+1}-O-, -N(C(O)R)S(O)_p-, -N(R)S(O)_pN(R)-, -N(R)-C(O)-(CH₂)_n-O-, -C(O)N(R)C(O)-, -S(O)_pN(R)C(O)-, -OS(O)_pN(R)-, -N(R)S(O)_pO-, -N(R)S(O)_pC(O)-, -SO_pN(C(O)R)-, -N(R)SO_pN(R)-, -C(O)O-, -N(R)P(OR_b)O-, -N(R)P(OR_b)-, -N(R)P(O)(OR_b)O-, -N(R)P(O)(OR_b)-, -N(C(O)R)P(OR_b)O-, -N(C(O)R)P(OR_b)-, -N(C(O)R)P(O)(OR_b)O-, or -N(C(O)R)P(OR_b)-;

20 where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_b for each occurrence is independently H, substituted or unsubstituted alkyl,

substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2; or

in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R

5 and R_b together form a five- or six-membered heterocyclic ring; or

A is NRSO₂ and R, R_a and the nitrogen atom together form a substituted or

unsubstituted five or-six-membered heterocyclic ring fused to ring 1; or

Z¹¹⁰-A-Z¹¹¹ taken together is a covalent bond; and

R₂ is a group of the formula -Z¹⁰¹-Z¹⁰²;

10 Z¹⁰¹ is a covalent bond, -(C₁-C₆)-, -(C₁-C₆)-O-, -(C₁-C₆)-C(O)-, -(C₁-C₆)-C(O)O-, -(C₁-C₆)-C(O)-NH-, -(C₁-C₆)-C(O)-N((C₁-C₆))- or a substituted or unsubstituted phenyl group;

Z¹⁰² is a substituted, saturated or unsaturated heterocyclic group; or a substituted,

15 saturated or unsaturated heterobicyclic group; wherein said substituted heterocyclic and substituted heterobicyclic group have one or more substituents each independently selected from the group consisting of nitro, halo, substituted or unsubstituted (C₁-C₆), substituted or

unsubstituted aryl, substituted or unsubstituted -C(O)-alkyl, substituted or unsubstituted -N(R)-(C₁-C₆)-OR, substituted or unsubstituted -N((C₁-

20 C₆)-OR)₂, substituted or unsubstituted -N(R)-(C₁-C₆)-C(O)₂R,

substituted or unsubstituted -(C₁-C₆)-N(R)-(C₁-C₆)-OR, substituted or unsubstituted -(C₁-C₆)-N(R)-(C₁-C₆)-N(R)₂, substituted or unsubstituted -(C₁-C₆)-C(O)N(R)-(C₁-C₆)-N(R)₂, substituted or unsubstituted -N(R)-(C₁-C₆)-OR, and a substituted or unsubstituted heterocyclic group

25 comprising one or more heteroatoms selected from the group consisting of O, and S; wherein the nitrogen atoms of said heterocyclic group or

- heterobicyclic group are independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted -C(O)N(R)₂, substituted or unsubstituted -C(O)-(C₁-C₆)-N(R)₂, -C(O)-alkyl, -C(O)-aryl, -C(O)-heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl;
- 5 a is 1 and D₁, G₁, J₁, L₁ and M₁ are each independently selected from the group consisting of CR_a and N, provided that at least two of D₁, G₁, J₁, L₁ and M₁ are CR_a; or
- 10 a is 0, and one of D₁, G₁, L₁ and M₁ is NR_a, one of D₁, G₁, L₁ and M₁ is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;
- b is 1 and D₂, G₂, J₂, L₂ and M₂ are each independently selected from the group consisting of CR_a and N, provided that at least two of D₂, G₂, J₂, L₂ and M₂ are CR_a; or
- 15 b is 0, and one of D₂, G₂, L₂ and M₂ is NR_a, one of D₂, G₂, L₂ and M₂ is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and
- n for each occurrence is independently an integer from 0 to 6;
- 20 provided that when A is -N(R)-, Z¹¹⁰ and Z¹¹¹ are each a covalent bond, and R₂ is a 3,4-diacyloxytetrahydrofur-2-yl, then Z¹⁰⁰ is not alkyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl or pyrrolidinyl;
- provided that when Z¹¹⁰ and Z¹¹¹ are each a covalent bond, and R₂ is a 3,4-diacyloxytetrahydrofur-2-yl, Z¹⁰⁰ is a substituted or unsubstituted alkyl,
- 25 then A is not alkyl, -O-, -C(O)-, -NHC(O)- or -C(O)O-;
- provided that when Z¹¹⁰-A-Z¹¹¹ taken together are a covalent bond, then Z¹⁰⁰ is

not alkyl; and
provided that when Z^{110} -A- Z^{111} taken together are a C_1 - C_6 alkyl, then Z^{100} is not
phenyl, pyrrolyl, imidazolyl, pyrazolyl, pyridinyl, pyrimidinyl,
pyrazinyl, pyridazinyl, furyl or thienyl.

5

113. A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

10

114. The method of Claim 113 wherein said protein kinase is selected from the group consisting of KDR, FGFR-1, PDGFR β , PDGFR α , IGF-1R, c-Met, Flt-1, Flt-4, TIE-2, TIE-1, Lck, Src, fyn, Lyn, Blk, hck, fgr and yes.

15

115. A method of affecting hyperproliferative disorders in a patient comprising administering a therapeutically effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

20

116. A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.

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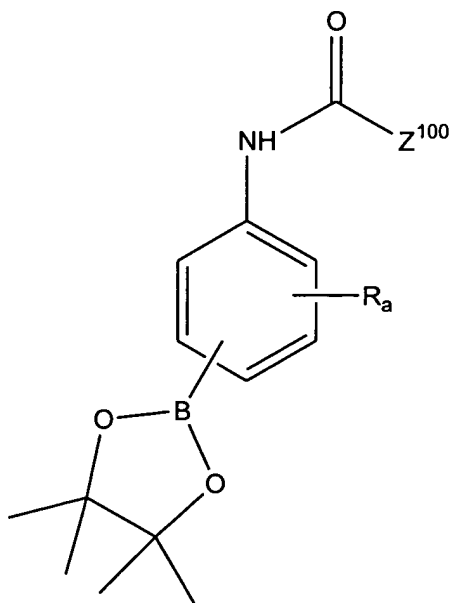
117. The method of Claim 113 wherein the protein kinase is a protein serine/threonine kinase or a protein tyrosine kinase.

118. A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient.
119. The method of Claim 118 wherein the ulcer or ulcers are caused by a bacterial or fungal infection; or the ulcer or ulcers are Mooren ulcers; or the ulcer or ulcers are a symptom of ulcerative colitis.
120. A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolites thereof to said patient, wherein said condition is an ocular condition, a cardiovascular condition, a cancer, Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell anaemia, chronic inflammation, systemic lupus, glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.

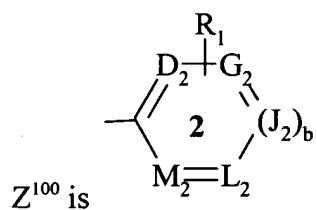
121. The method of Claim 120 wherein the ocular condition is ocular or macular edema, ocular neovascular disease, scleritis, radial keratotomy, uveitis, vitritis, myopia, optic pits, chronic retinal detachment, post-laser treatment complications, conjunctivitis, Stargardt's disease, Eales disease, retinopathy or macular degeneration.
122. The method of Claim 120 wherein the cardiovascular condition is atherosclerosis, restenosis, ischemia/reperfusion injury, vascular occlusion or carotid obstructive disease.
123. The method of Claim 120 wherein the cancer is a solid tumor, a sarcoma, fibrosarcoma, osteoma, melanoma, retinoblastoma, a rhabdomyosarcoma, glioblastoma, neuroblastoma, teratocarcinoma, an hematopoietic malignancy, Kaposi's sarcoma, Hodgkin's disease, lymphoma, myeloma, leukemia or malignant ascites.
124. The method of Claim 120 wherein the diabetic condition is insulin-dependent diabetes mellitus glaucoma, diabetic retinopathy or microangiopathy.
125. A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 89, 101, 107, 108, 109, 110, 111 or 112 or a physiologically acceptable salt, prodrug or biologically active metabolite thereof.

126. The method of Claim 116 wherein the compound or a physiologically acceptable salt, prodrug or biologically active metabolite thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.
- 5 127. The method of Claim 114 wherein the protein kinase is Tie-2.
128. The method of Claim 126 wherein the compound of Formula I, or physiologically acceptable salt, prodrug or biologically active metabolite thereof, is administered in combination with a pro-angiogenic growth factor.
- 10 129. The method of Claim 128 wherein the pro-angiogenic growth factor is selected from the group consisting of VEGF, VEGF-B, VEGF-C, VEGF-D, VEGF-E, HGF, FGF-1, FGF-2, derivatives thereof and antiidotypic antibodies.
- 15 130. The method of Claim 126 wherein the patient is suffering from anemia, ischemia, infarct, transplant rejection, a wound, gangrene or necrosis.
131. The method of Claim 113 wherein the protein kinase activity is involved in T cell activation, B cell activation, mast cell degranulation, monocyte activation, the potentiation of an inflammatory response or a combination thereof.
- 20 132. A method of preparing a 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl intermediate represented by the following structural formula:

-1034-



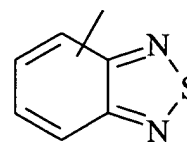
wherein:

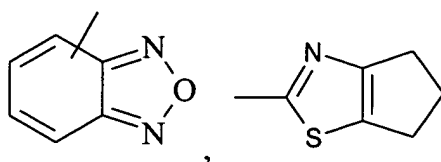


or a group optionally substituted with R₁ selected from

the group consisting of alkyl, cycloalkyl, pyrrolidinyl, quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, phthalazinyl, imidazo[1,2-a]pyrimidinyl, 1H-imidazo[1,2-a]imidazolyl, imidazo[2,1-b][1,3]thiazolyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl,

thienyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl,





5 , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, pyrrolopyridinyl, H-pyridinone, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl, imidazo[1,2-a]pyridinyl, benzoisothiazolyl, 1,1-dioxybenzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

R_a and R_i represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO₂, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, -C(O)O-aryl, -C(O)O-heteroaryl, -C(O)-alkyl, -C(O)-aryl, -C(O)-heteroaryl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted heteroarylalkoxy, substituted or unsubstituted arylalkoxy, substituted or unsubstituted alkyl-S(O)_p-, substituted or unsubstituted alkyl-S-, substituted or unsubstituted aryl-S(O)_p-, substituted or unsubstituted heteroaryl-S(O)_p-, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted

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aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, $-Z^{105}-C(O)N(R)_2$, $-Z^{105}-N(R)-C(O)-Z^{200}$, $-Z^{105}-N(R)-S(O)_2-Z^{200}$, $-Z^{105}-N(R)-C(O)-N(R)-Z^{200}$, R_c and CH_2OR_c ;

5 where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, $-CH_2-NR_dR_e$, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t-O$ -alkyl, $-W-(CH_2)_t-S$ -alkyl, or $-W-(CH_2)_t-OH$; Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6) ;

10 Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted phenyl or substituted or unsubstituted $-(C_1-C_6)$ -phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2 -alkyl; or R_d , R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring;

15 t for each occurrence is independently an integer from 2 to 6;

W for each occurrence is independently a direct bond or O, S, $S(O)$, $S(O)_2$, or NR_p , wherein R_f for each occurrence is independently H or alkyl; or

R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2; and

20 R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

p is 1 or 2; and

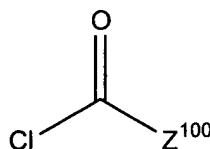
b is 1 and D_2 , G_2 , J_2 , L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2 , G_2 , J_2 , L_2 and M_2 are CR_a ; or

25 b is 0, and one of D_2 , G_2 , L_2 and M_2 is NR_a , one of D_2 , G_2 , L_2 and M_2 is CR_a and

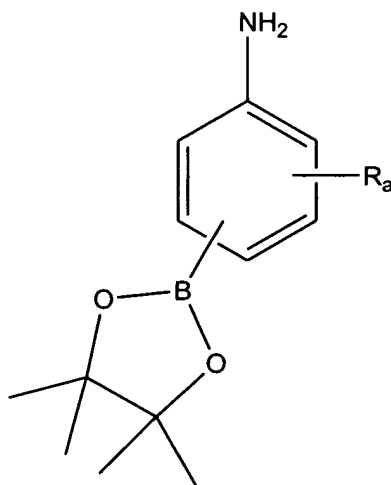
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the remainder are independently selected from the group consisting of CR_a and N , wherein R_a is as defined above;
 comprising the step of reacting in the presence of an aprotic base an acid chloride represented by the following structural formula:

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with a (4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)aniline represented by the following structural formula:



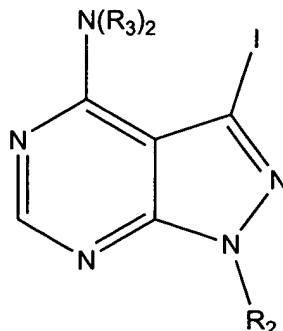
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to form said 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl intermediate.

133. The method of Claim 132, further comprising the step of reacting the 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl intermediate in the presence of

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tetrakis(triphenylphosphine)palladium(0) and sodium carbonate with a 3-iodo-1*H*-pyrazolo[3,4-*d*]pyrimidine represented by the following structural formula:



5 wherein:

R_2 is H or a group of the formula $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;

10 Z^{102} is hydrogen; a substituted or unsubstituted alkyl group; a substituted or unsubstituted cycloalkyl group; a substituted or unsubstituted cycloalkenyl, a substituted or unsubstituted, saturated or unsaturated heterocyclic group; or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group; wherein said substituted alkyl, substituted cycloalkyl, substituted cycloalkenyl, substituted heterocyclic and substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, nitro, halo, substituted or unsubstituted (C_1-C_6) , substituted or unsubstituted aryl, substituted or unsubstituted $-C(O)-$ alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-N((C_1-C_6)-OR)_2$, substituted or

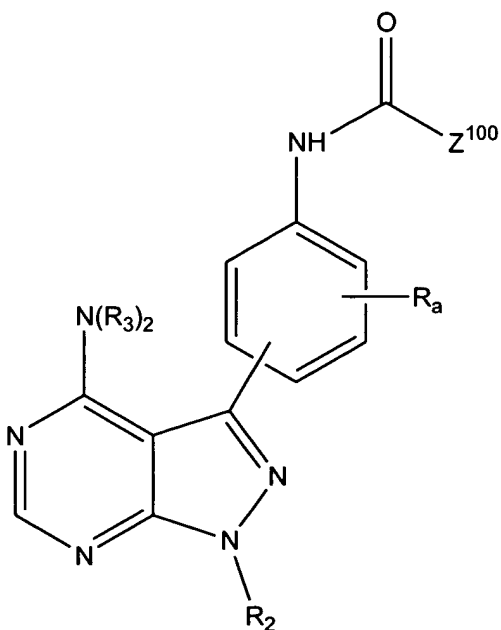
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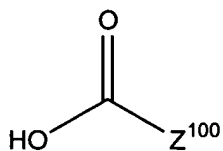
- unsubstituted $-N(R)-(C_1-C_6)-C(O)_2R$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-OR$, substituted or unsubstituted $-(C_1-C_6)-N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted $-(C_1-C_6)-C(O)N(R)-(C_1-C_6)-N(R)_2$, substituted or unsubstituted sulfonamido, substituted or
 5 unsubstituted ureido, substituted or unsubstituted carboxamido, substituted or unsubstituted amino, substituted or unsubstituted $-N(R)-(C_1-C_6)-OR$, oxo, and a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more heteroatoms selected from the group consisting of N, O, and S; wherein the nitrogen
 10 atoms of said heterocyclic group or heterobicyclic group are independently optionally substituted by oxo, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted $-C(O)N(R)_2$, substituted or unsubstituted $-C(O)-(C_1-C_6)-N(R)_2$, $-C(O)-alkyl$, $-C(O)-aryl$, $-C(O)-$
 15 heteroaryl, substituted or unsubstituted arylalkyl group, or substituted or unsubstituted heteroarylalkyl; or
 R_2 is a group of the formula $-B-E$, wherein B is a substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted azacycloalkyl, substituted or
 20 unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalkylcarbonyl, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylencarbonyl or substituted or
 25 unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, substituted

or unsubstituted azacycloalkyl, a substituted or unsubstituted
 heterocycloalkyl, substituted or unsubstituted (C₁-C₆)-azacycloalkyl-,
 substituted or unsubstituted azacycloalkylcarbonyl, substituted or
 unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted
 5 azacycloalkylalkyl, substituted or unsubstituted heteroaryl-N(R)-(C₁-C₆)-
 , substituted or unsubstituted aryl-N(R)-(C₁-C₆)-, substituted or
 unsubstituted alkyl-N(R)-(C₁-C₆)-, substituted or unsubstituted
 heteroaryl-(C₁-C₆)-N(R)-, substituted or unsubstituted aryl-(C₁-C₆)-N(R)-
 , substituted or unsubstituted alkyl-(C₁-C₆)-N(R)-, substituted or
 10 unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl,
 substituted or unsubstituted alkylcarbonyl, substituted or unsubstituted
 arylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted
 or unsubstituted alkylsulfonyl, substituted or unsubstituted arylsulfonyl,
 substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted
 15 arylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino,
 substituted or unsubstituted heteroarylcarbonylamino, substituted or
 unsubstituted arylcarbonylamino, substituted or unsubstituted
 alkylcarbonylamino or substituted or unsubstituted aryl; and
 R₃ for each occurrence is, independently, hydrogen, hydroxy, substituted or
 20 unsubstituted alkyl, substituted or unsubstituted -C(O)-alkyl, a
 substituted or unsubstituted -C(O)-aryl, or a substituted or unsubstituted
 -C(O)-heteroaryl or substituted or unsubstituted alkoxy;
 to form a compound represented by the following structural formula:

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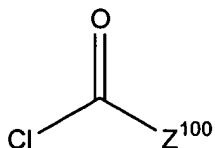


134. The method of Claim 133, further comprising the step of reacting a carboxylic acid represented by the following structural formula:



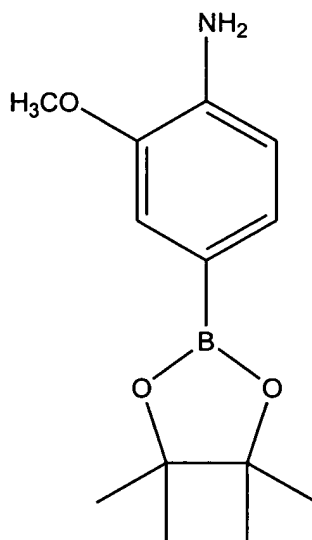
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with oxalyl chloride and an aprotic base to form an acid chloride represented by the following structural formula:

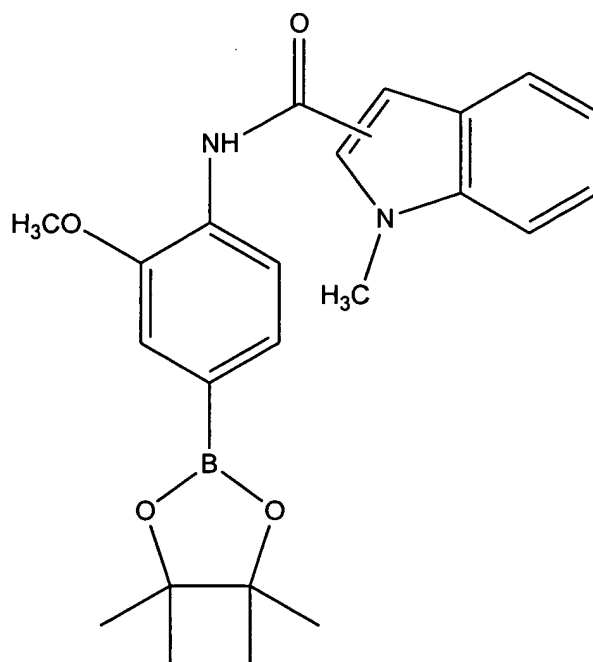


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135. The method of Claim 132, 133 or 134 wherein Z^{100} is an indolyl which is optionally substituted with R_1 .
136. The method of Claim 135, wherein Z^{100} is 1-methyl-indol-2-yl or 1-methyl-indol-3-yl.
137. The method of Claim 136, wherein the (4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl)aniline is represented by the following structural formula:



and the 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl intermediate is represented by the following structural formula:



138. The method of Claim 137, wherein R_2 is 4-(4-methylpiperazino)cyclohexyl.